

Lars Lindholm

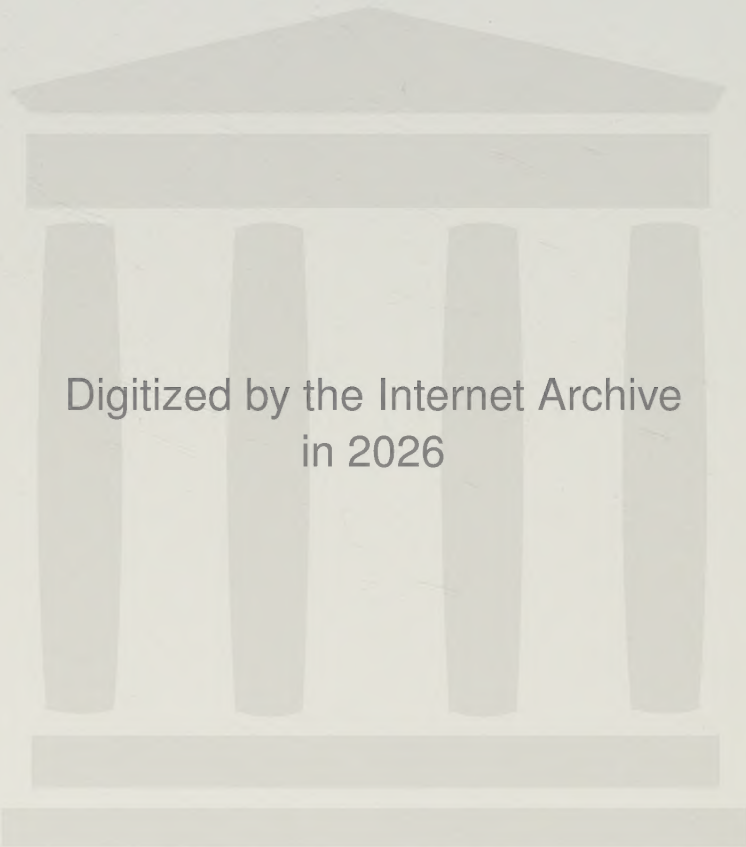
Hypertension and its Risks

Epidemiological Studies in Swedish Primary
Health Care



Dalby, 1984

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HYPERTENSION AND ITS RISKS

Epidemiological studies in Swedish Primary Health Care

av

Lars Lindholm

Med lic, Mlm

AKADEMISK AVHANDLING

som med vederbörligt tillstånd av Medicinska Fakulteten i Lund för avläggande av medicine doktorsexamen kommer att offentligen försvaras i föreläsningssalen, Institutionen för klinisk samhällsmedicin, Vårdcentralen i Dalby, lördagen den 19 maj 1984 klockan 9.15.

Dalby 1984

Organization LUND UNIVERSITY Department of Community Health Sciences S-240 10 Dalby, Sweden	Document name DOCTORAL DISSERTATION	
	Date of issue April 1984	
	CODEN: LUMEDW/(MECH-1002)/1-157(1984)	
Author(s) Lars Lindholm	Sponsoring organization	
Title and subtitle HYPERTENSION AND ITS RISKS Epidemiological Studies in Swedish Primary Health Care		
Abstract The purpose of this study was to analyse if epidemiological research models concerning risks of hypertension could be applied to the limited numbers of people in a primary care district and yet give valid results. The study has shown: - that our male hypertensives below the age of 70 years had high risks of cerebro-cardiovascular diseases (CCVD) even though they had been subjected to an extensive anti-hypertensive program, their blood pressure values had been reduced in accordance with what has been internationally accepted, 75 % of them attained their treatment objectives and their smoking habits had been reduced; - that hypertension in obese parents was a stronger risk indicator of hypertension in offspring than was parental hypertension itself; - that isotonic regression analysis of blood pressure on age was an adequate technique to define study groups for mortality analysis in a moderately sized population, where blood pressure increases with age; - that both high and low blood pressures in men were found to be risk indicators of death and that an inhomogeneity was likely in both the lowest and the highest blood pressure quintile; - that limited numbers of people in a defined population can be utilized in epidemiological studies regarding risk and thus justify our models for studies in primary health care; We <u>conclude</u> that we are faced with a complex problem concerning prevention of CCVD in our hypertensives since they have high risks even though they are adequately treated. Should we increase their drug therapy, reduce their weight and alcohol consumption, interfere with metabolic factors or with quite other - nonbiological - factors? These are questions which merit further studies.		
Key words Alcohol, blood pressure, cardiovascular disease, death rate, elderly, family history, gamma-glutamyl-transferase, hypertension, isotonic regression, nurses, obesity, prospective studies, retrospective studies, smoking, stroke.		
Classification system and/or index terms (if any)		
Supplementary bibliographical information		Language English
ISSN and key title		ISBN
Recipient's notes	Number of pages 157	Price
	Security classification	

Distribution by (name and address)

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April 1984

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Hypertension and its Risks

Epidemiological Studies in Swedish
Primary Health Care

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Dalby, Sweden

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Hypertension and its Risks

Epidemiological Studies in Sweden
Volume 1: The Cohort

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Printed in Sweden
Studentlitteratur
Lund 1984

To Lena-Pia, Annika and Sara-Lotta
with my love and affection

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LIST OF PUBLICATIONS

This thesis is based on the following papers, which will be referred to by their roman numerals:

- I. Lindholm L. Efficacy of a district nurse program in follow-up of hypertensives. A two-year single-group study in a Swedish primary care district. *Family Practice - An International Journal*; (Oxford University Press). In press, 1984.
- II. Lindholm L, Ejlerstsson G, Scherstén B. High risks of cerebro-cardio-vascular morbidity in well treated male hypertensives. A retrospective study of 40-59-year-old hypertensives in a Swedish primary care district. *Acta Med Scand*. In press, 1984.
- III. Lindholm L, Scherstén B, Thulin T. Hypertension in elderly people in a Swedish primary care district. *Scand J Prim Health Care* 1983; 3-4: 120-131.
- IV. Lindholm L. Parental obesity combined with hypertension - an indicator of excess risk of hypertension in offspring. A case-control study in a Swedish primary care district. *Acta Med Scand*. In press, 1984.
- V. Lindholm L, Lithman T. Impact of hypertension on a defined population: Utility of a population based case-control study model of limited numbers in estimating risks. Submitted for publication.
- VI. Lindholm L, Lanke J, Bengtsson B, Ejlerstsson G, Thulin T, Scherstén B. Both high and low blood pressures found to be risk indicators of death. Isotonic regression of blood pressure on age applied to data from a thirteen-year prospective study on males. Submitted for publication.

1. INTRODUCTION

High blood pressure is a serious risk criterion of cerebro-cardiovascular morbidity and mortality below the age of 70 years, especially if other risk indicators such as smoking, obesity, high cholesterol and/or excessive alcohol consumption are also present (1-2). The risks of morbidity and mortality increase with pressure and there is no clearly defined cut-off point for increased risk, since blood pressure is a unimodal and continuous variable (3).

Lowering of high blood pressure is one effective way of reducing morbidity and mortality in both established (4-12) and mild (13-21) hypertension.

Multifactorial intervention programs on high-risk individuals as well as high-risk populations have been carried out and some have reported beneficial effects on cardiovascular morbidity and mortality after control of hypertension and adoption of better life styles (22-24). In one study (MRFIT), however, an intervention on hypertension, hyperlipidaemia and smoking was carried out, leading to a reduction of these risk indicators but not to any difference in the reduction of mortality when the group receiving special care was compared with the group referred to usual care (25).

Regarding those aged over 70 years, few studies have been reported on morbidity and mortality of patients with hypertension. Whether or not pharmacological lowering of high blood pressure in this age group can reduce morbidity and prolong life is still a controversial question.

Management programs with uniform guidelines for clinical work-up, treatment and follow-up of hypertensives have been put into effect in various parts of Sweden in order to make treatment more effective (26,27). The basis for these programs has been constructed by the National Board of Health and Welfare and other authorities (28).

The primary health care services have a responsibility for the health and medical treatment of the population in a defined district (29) and ought to form the basis for the long-term management and follow-up of patients with actual and borderline hypertension in Sweden (28).

Since the primary health services will be responsible for the treatment of hypertensives, it is important that research into hypertension is also carried out within primary health care to find new methods for screening, treatment and follow-up of the hypertension as well as to analyse the effect of treatment.

Epidemiological research models which can be applied to the limited numbers of people in each catchment district in primary health care and yet give valid results must therefore be tested and compared with larger studies. In the light of these considerations the present investigation was initiated as described below in "Background".

2. BACKGROUND

2.1 The study area

The Dalby primary care district is situated in southwest Sweden, in the County of Malmöhus. The district had about 21,000 inhabitants in January 1983. It consists of four villages (Dalby, Genarp, Veberöd and Sandby), each having a small surgery for district nurses. There was only one Health (Care) Centre (Dalby) in the district in 1968-1981 but a second one (Sandby) opened in 1982, affiliated to Dalby. The primary health care service is staffed by eight district physicians, eight district nurses as well as auxiliary staff (e.g. nurses, midwives, occupational therapist and physiotherapists). Since 1968 a unit for research in primary health has been located at Dalby and since 1981 this has been incorporated into the University of Lund as a Health Sciences Centre.

2.2 Out-patient and in-patient computer schemes

All inhabitants in the primary care district are identified by their civic registration numbers and are listed in order of birth in the official population register for the Dalby district, comprising all its population.

Since the Health Centre opened in 1968, data on all patients regarding diagnoses, blood pressure, laboratory test results, and ECG have been registered in an out-patient computer scheme which can be described as an individually based computer system for the processing of statistical information about the patients and their contacts with the health and medical services (30).

Information about the in-patient treatment has been gathered since 1969 by means of the computer scheme for in-patient care in the County of Malmöhus. This scheme gathers information from all hospitals in the County regarding patients admitted (31).

In both schemes the patients are registered by their civic registration numbers and the diagnoses according to the ICD (International Statistical Classification of Diseases) codes (32). Since 1977 an abbreviated version of this classification is used for out-patient care (33).

2.3 Earlier activities regarding blood pressure in Dalby

The Dalby district has been the subject of great interest regarding blood pressure during the last decade. In 1969, the blood pressure of the inhabitants in

Dalby village was recorded (34-35). A few years later a clinic for hypertensives was organized within the Health Centre. It has been run by a specially trained nurse for more than ten years. In this clinic the nurse sees the hypertensives between visits to the district physicians. She records their blood pressure, instructs them regarding diet and medication, checks compliance and follows up laboratory tests according to the regional management program for hypertension. About half of all known hypertensives in the district were registered at this clinic in 1981, while the remainder received regular care, mostly from the district physicians.

In 1975-76 an extensive educational program on hypertension was organized within the County of Malmöhus. All district physicians and district nurses in the area were invited to this continuing education, in which most participated.

The district nurses' surgeries were thereafter equipped with mercury manometers and cuffs of different sizes (12 x 35 cm, 15 x 43 cm).

In 1980, many adequately treated hypertensives above the age of 50 years attended the clinic for hypertensives at the Health Centre at regular intervals, to have their blood pressure recorded between visits to the district physicians. Because of insufficient public transportation some even came by taxi to these appointments. When asked, several patients stated that they would have preferred to have had their blood pressure recorded by the district nurse in the village where they lived.

District nurses seem to be taking on increasingly important duties both in prevention and in the care of patients with chronic diseases, but few studies have reported on the efficacy of district nurse programs in the follow-up of these patients. A study was therefore performed to investigate whether hypertensives above the age of 50 years and with blood pressure under satisfactory control could be referred to district nurses for their follow-up between visits to the district physicians, without risking loss of control over their blood pressure.

2.4 Study of the efficacy of a district nurse program in follow-up of hypertensives (paper I)

Hypertensives often suffer with complex health problems, having social aspects for which they consult the district nurses, who have their surgeries near the patients' homes and are well known to them. It has been found that the

inhabitants in a primary care district were well aware of the district nurses' daily services, and were positive toward them (36). More than 90 % regarded measurement of blood pressure as one of the district nurses' tasks. It has also been shown that most aspects of the management of hypertensives can be delegated to specially trained nurses who, providing they accept rational objectives and maintain routine, generally achieve better results than more highly trained medical staff, who do not (37-39).

A two-year single-group study was performed and the following questions were asked:

- Do the referred patients visit the district nurse as scheduled?
- Do the patients continue the follow-up throughout the observation period?
- Do the patients return to the district physician as scheduled?
- Do the patients keep their blood pressure equal to or below the treatment objective?

The initial attendance rate at the nurse's was high (78-92 %), but the tendency to continue the follow-up was lower (36-51 %). Lack of information was the major reason for patients' discontinuing the follow-up without acceptable reason. Most non-attenders had concomitant chronic diseases and visited the Health Centre because of these. About 90 % of all patients returned to the district physicians as scheduled. Most attenders attained their treatment objective during the study.

Comments

Hypertensives above the age of 50 years whose blood pressure is under satisfactory control and who do not require regular visits to the Health Centre for other chronic diseases may be referred to district nurses for follow-up, without risking loss of control over their blood pressure. However, the study emphasizes the importance of giving repeated information to the hypertensives about the scheduled follow-up program. The existing medical services were used in this study. Thus, it is applicable to the future 'team model' of primary health care. It may be compared to the model used in the County of Skaraborg, Sweden (26) where clinics with specially trained nurses for the treatment and follow-up of hypertensives were organized in primary health care. That model showed very good results regarding control of hypertensives but is not feasible, however, in the County of Malmöhus where primary health care in the future will be organized by district physicians and nurses working in teams.

The Dalby clinic for hypertensives has been integrated with the clinic for diabetics, since there seems to be a greater future need for specially trained nurses for the care of diabetics than of hypertensives. Patients with uncontrolled hypertension and young hypertensives are still registered at this clinic.

In the light of the earlier studies and activities regarding blood pressure in the Dalby population, during the last decade, as well as results from other investigations (22-26) we found it of interest to study the efficacy of the existing treatment and follow-up program for hypertensives. This was performed by using the out-patient and in-patient computer schemes.

3. AIMS

3.1 General aim

The purpose of this investigation was to analyse if epidemiological research models concerning risks of hypertension could be applied to the limited numbers of people in a primary (health) care district and yet give valid results.

3.2 Specific aims

- to investigate whether our hypertensives were adequately treated and to analyse the risks of cerebro-cardiovascular morbidity and its determinants such as smoking, alcohol drinking habits, obesity, family history etc.
- to investigate the prevalence of hypertension in the district in order to study the extent of the problem and to what degree hypertension was undiagnosed.
- to analyse the impact of hypertension on a population subjected to an extensive anti-hypertension program.
- to analyse if the existing in-patient and out-patient computer schemes could be used for retrospective and prospective studies regarding risk.
- to analyse the prognostic value of a 'casual' blood pressure on the male inhabitants in a primary care district.

4. METHODS AND EPIDEMIOLOGICAL CONSIDERATIONS

4.1 Retrospective studies

4.1.1 Studies on the efficacy of treatment on 40-69-year-old hypertensives (papers II, III, IV)

Study groups

To investigate whether our hypertensives were adequately treated, all patients born in 1912-41 who visited the Dalby Health Centre in 1980 because of actual or borderline hypertension ($n = 313$) were identified by means of the out-patient computer scheme in Dalby. They were invited to a medical examination in 1981, including a structured interview, laboratory tests, weight and height measurements, blood pressure recordings and a conventional clinical examination by a physician. Of all invited patients, 300 (96 %) attended the examinations. They were divided into two groups - hypertensives and borderline hypertensives - according to the diagnosis in their medical records based on the criteria mentioned below.

The patients were compared with an age- and sex-matched control group, chosen from the same primary care district with the aid of the official population register. All inhabitants in the primary care district were listed in chronological birth date order in this register, as mentioned above. For each patient who attended the examinations, two persons of the same sex, located immediately before and after the patient in the population register, were selected as controls. In this way 600 control persons should have been selected but since 28 controls were shared by patients near each other in the register, only 572 controls were invited. They were born the same year and month as the patients and mostly also on the same day and comprised the **control material**, of whom 476 (83 %) attended the examinations. Controls who had a diagnosis of hypertension or borderline hypertension as well as those who had a systolic blood pressure exceeding 155 mm Hg (age group 40-59 years) or 165 mm Hg (age group 60-69 years) and/or a diastolic blood pressure exceeding 90 mm Hg (age group 40-59 years) or 100 mm Hg (age group 60-69 years) at either of two examinations - on separate days - were not accepted in the analyses of hypertensives vs. non-hypertensive controls. Altogether 159 control persons were excluded. Thus, the **control group** amounted to 317 persons (Fig. 1, paper II; Fig. 1, paper III). Comparisons were made between the group of patients and the group of controls.

Organization

Patients and controls were first interviewed by a single specially trained nurse concerning their family history, medication and their smoking as well as alcohol habits. Blood pressure was measured in both arms after 5-10 minutes of rest in a recumbent position and in the right arm after 2 minutes' standing. Diastolic blood pressure values were phase V. All measurements were made with the same equipment which was checked by technicians at regular intervals. Cuffs of different sizes (9 x 28, 12 x 35, 15 x 43 cm) were used.

Blood samples were drawn at random with standard Vacutainer technique and were analysed at the Department of Clinical Chemistry, Lund University Hospital. For details, see papers II and III. Serum gamma-glutamyltransferase (S-GT, $\mu\text{Kat/l}$) was chosen as an indicator of alcohol consumption. Body weight in underwear (w, kg) and height (h, m) were measured, and the body mass index (w/h^2) was calculated.

All patients and controls were seen by a physician who made a conventional clinical examination. Anamnestic data, including past history of diseases, were recorded for all attenders, at a structured interview, and were checked against the medical records at the Health Centre, at the University Hospital and at private practitioners when indicated.

Estimation of parental obesity

All patients and controls were mailed a questionnaire after the examination, in which they were asked to rate their parents as very fat, fat, normal, thin or very thin when middle-aged (paper IV). The questionnaire was returned by 92 %. This was performed to estimate the degree to which parental obesity affected the risk of hypertension in offspring.

The validity of the questionnaire was examined in 40 cases (hypertensives) and controls (non-hypertensives). The youngest ones were chosen, as their parents were in most cases still below 70 years of age. These cases and controls were mailed a second questionnaire (after having answered the first one) in which they were asked to state their parents' present age; weight and height. The results of the validity study in both parents are shown separately for patients and controls in Fig. 1. Only two categories of the scale were used by those who took part in the validity study - fat and normal weight. Therefore all parents were categorized as either obese (including very fat and fat) or non-obese (including normal, thin and very thin) in the subsequent analyses.

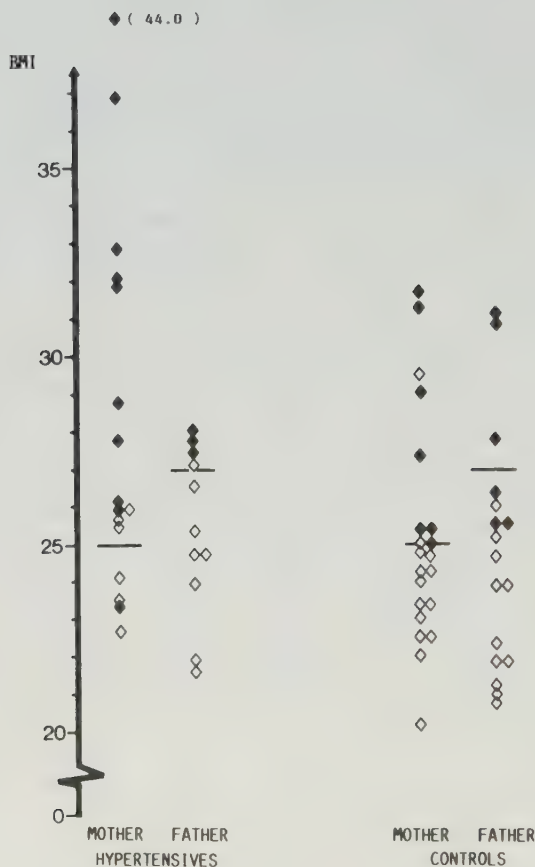


Figure 1. Body mass index (BMI) in parents, related to body weight estimated by their offspring (hypertensives and controls) as obese ◆ and non-obese ◇.

Criteria for diagnoses of hypertension and borderline hypertension

At the Health Centre in Dalby the blood pressure limits used in the daily routine for asymptomatic patients aged 40-59 years were (mean of at least three measurements): for hypertension $> 170 / > 105$ mm Hg and for borderline hypertension 160-170/95-105 mm Hg. The corresponding limits for the age group 60 years and above, were $> 180 / > 110$ mm Hg and 170-180/105-110 mm Hg, respectively. If the patient had diabetes the limits were 5-10 mm Hg lower.

Objective of treatment

The aim of treatment in the age group 40-59 years was to establish a level of $\leq 160/\leq 95$ mm Hg. In the age group 60 years and above, the corresponding objective was $\leq 180/\leq 100$ mm Hg. In diabetics the aim was generally 5-10 mm Hg lower.

Non-attending patients and controls

For the few patients who failed to attend the examinations, information was obtained from the medical records. Information was also obtained on 76-82 % of the non-attending controls from records at the Lund University Hospital as well as at the Health Centre. The prevalence of CCVD did not differ when attending controls were compared with non-attenders (papers II and III). We have no information about the non-attenders' parents, but see no reason why they should differ from the attenders' (paper IV).

Representativity of the hypertensive patients

From our analyses of the **control material** we have estimated that about 85 % of all known hypertensives in the district aged 60 years and above, and about 60-65 % of those aged 40-59 years, were included in our group of patients. Our analyses indicated that these patients were representative of all hypertensives in the primary care district (papers II and III).

Data processing and statistical methods

All data were stored, structured and analysed by using the SPSS Program System on a large Univac Computer 1100/80. Student's t -test (two-tailed) was used to test the hypothesis of no difference in mean values between two groups and to test the hypothesis of no correlation between variables. The normal deviate test was used to test the hypothesis of no difference between proportions where the normal distribution was used as an approximation of the binomial distribution.

In order to test the difference between frequencies in two or more groups the Chi-square test was used. Yates' correction for continuity was used where any of the expected frequencies was less than five, for one degree of freedom.

Partial correlation analysis was used to describe the linear relationship between two variables when the influence of other variables had been eliminated, in

paper II. These results were expressed as partial correlation coefficients. The dependent variable was blood pressure group and the independent variables were body mass index, age, alcohol habits, smoking habits and S-GT, chosen as an indicator of alcohol consumption (40). Since blood pressure was measured on an ordinal scale, the relationship between S-GT and blood pressure group was checked with an analysis of variance. In a multiple regression analysis the correlation between the dependent variable and all independent variables was compared.

In the epidemiological estimations of relative odds described below, the 95 % confidence interval was calculated as described by Lilienfeld (Haldane's method), (41).

Statistical significance was evaluated at the levels $p < 0.05$, < 0.01 and < 0.001 . A difference was considered significant when the p-value was < 0.05 .

A considerable number of statistical analyses were performed and the concept of mass significance must therefore be remembered.

Since the studies comprised small numbers the risk of a type II fallacy was considered when the results showed no difference between the groups.

Epidemiological considerations

Retrospective studies on hypertensives vs. non-hypertensive controls were performed with care. The controls were matched with the patients with regard to sex, age, race and residential area (all living in the same suburban primary care district). All attenders were asked about their past history of CCVD and their answers were checked against the medical records as described above. The relative odds of a CCVD was estimated as shown in Fig. 2. These estimates were relevant since both patients and controls were selected in a known way and from the same population, as described above.

This study model was chosen, as it made possible analyses and inter-group comparisons of blood pressure, laboratory test results, body mass index, alcohol- and smoking habits. It was also possible to calculate the percentage of patients who attained their treatment objectives (papers II and III) and to compare hypertensives with vs. without CCVD (paper II).

	Hypertensives	Controls
CCV disease	a	b
No CCV disease	c	d

$$\psi = \frac{\frac{a}{c}}{\frac{b}{d}} = \frac{a \cdot d}{c \cdot b}$$

$$\psi_c = \frac{(a + 0.5) \cdot (d + 0.5)}{(c + 0.5) \cdot (b + 0.5)}$$

Figure 2. Estimation of relative odds (ψ) and corrected relative odds (ψ_c) of cerebro-cardiovascular diseases (CCV) in hypertensives and controls; **a, b, c** and **d** indicate numbers.

When estimating the relative odds of a CCVD it must be emphasized that the study model in papers II and III cannot in all aspects be regarded as a true case-control study. In such a study, individuals with a particular condition or disease (the cases) are selected for comparison with a series of individuals in whom the condition or disease is absent (the controls). Cases and controls are compared with respect to existing or past attributes or exposures believed to be relevant to the development of the condition or disease being studied (41-43).

In paper IV, however, the study model can be regarded as a case control study e.g. of obesity (attribute) with regard to hypertension (disease). The estimates of relative odds in that study are shown in Fig. 3.

	Hypertensives	Controls
with characteristic	a	b
without characteristic	c	d

$$\psi = \frac{\frac{a}{b}}{\frac{c}{d}} = \frac{a \cdot d}{b \cdot c}$$

$$\psi_c = \frac{(a + 0.5) \cdot (d + 0.5)}{(b + 0.5) \cdot (c + 0.5)}$$

Figure 3. Estimation of relative odds (ψ) and corrected relative odds (ψ_c) of hypertension in persons with and without a characteristic; **a**, **b**, **c** and **d** indicate numbers.

In the retrospective study model used in papers II and III the risk of a CCVD may be underestimated, as hypertensives who had died of a CCVD before the study were not included. The study comprised only hypertensives who visited the Health Centre in 1980 and were alive at the end of that year. Patients and controls omitting information about their CCVD may also have influenced the results, but since their information was matched with the in-patient as well as out-patient computer schemes, this was of little importance and therefore ignored. When estimating relative odds, Lilienfeld recommends the practice of adding 0.5 to each value (**a**, **b**, **c** and **d** in Figures 2 and 3) to correct for a bias that can occur with small numbers of observations (41). Schlesselman, on the other hand, prefers to ignore this correction factor (42). We have chosen to use the correction for small numbers in order to avoid an overestimation of the risks. This also tallies with Haldane's method of calculating the 95 % confidence interval.

When estimating the prevalence of hypertension, the **control material** was used. In the age group 60-69 years the proportion of the population examined in each year group varied to a minor degree. Thus, the prevalence could be estimated without weighting, as shown in paper III. In the age group 40-59 years, however, the older age groups were overrepresented in the control material (since the prevalence of hypertension increases with age). Thus, the estimates of hypertension would have been too high if a weighting had not been performed. The prevalence of hypertension was weighted for the age groups 40-49 and 50-59 years according to the formula presented in paper IV.

4.1.2 Case-control study of the impact of hypertension on the population with regard to myocardial infarction and stroke (Paper V)

Study groups

All new patients having suffered myocardial infarction or stroke, born between 1912 and 1931 and diagnosed during the period 1973-82 among the inhabitants of the Dalby primary care district were identified by means of the in-patient computer scheme as well as the out-patient scheme described above. The numbers of patients identified in the two schemes were compared in paper V, Fig. 1. There was no clustering within the ten-year period. The medical records were sought and studied by a physician. Information regarding the patients' smoking habits and diagnosis of hypertension - if any - was extracted. In 10 cases out of 182 (5 %) the medical records could not be found, which may be attributable to incorrect filing.

From earlier studies (papers II, III, IV) we have obtained information about a **control material** representative of the population born in 1912-41 in our primary care district. This control material comprised 227 males and 250 females born in 1912-31, of whom 82 % attended examinations in 1981. The control material amounted to 16 % of all inhabitants in this age group in the district. It included 12 male patients with a history of myocardial infarction and 6 with stroke as well as 4 female patients with myocardial infarction and 1 with stroke. In this case-control study we have selected the controls from that control material. For each case we have selected a control person who was as close in age as possible and of the same sex. When selecting controls for patients with myocardial infarction, those with a history of myocardial infarction themselves were omitted. The same exclusion procedure was performed with regard to stroke. The controls were not chosen at the time of diagnosis of the cases, since the bias introduced by ignoring the matching with time may be considered negligible when

estimating risk (44). The controls' smoking habits as well as their diagnosis of hypertension - if any - were known from earlier studies. All comparisons were made between groups of cases and groups of controls.

Data processing and statistical methods

Data were analysed and statistical methods were used as described above for papers II-IV.

Epidemiological considerations

The 10-year incidence of myocardial infarction and stroke in subjects below 70 years of age was used to analyse the usefulness of a population-based case-control study model in a primary care district, where extensive studies and treatment programs regarding blood pressure have been performed during the last decade.

The population-attributable risk was estimated as shown in Fig. 4. It implies the impact that a specific exposure (hypertension) may have on the population with respect to a particular outcome (myocardial infarction or stroke). The concept of population-attributable risk is useful in that it provides an estimate of the amount by which myocardial infarction and stroke might be reduced in the population in a primary care district, if hypertension could be removed.

This study also considers patients who have died from myocardial infarction or stroke. We have no information, however, regarding patients who did not seek medical advice for these diseases (e.g. silent infarction) nor regarding those who died at home before being diagnosed. These groups have been considered by others (31,45,46), and each may amount to about 20 % of the cases or even more (47). In this study we have accepted the diagnoses made at Lund University Hospital. Most cases of myocardial infarction were diagnosed at the Department of Cardiology and thus according to WHO rules and almost all patients with stroke were diagnosed at the Department of Neurology. These departments have a special interest in patients with myocardial infarction and stroke, respectively. Only one patient was obviously mis-diagnosed and was therefore omitted.

	Cases	Controls
Hypertensives	a	b
Non-hypertensives	c	d

$$\psi = \frac{\frac{a}{b}}{\frac{c}{d}} = \frac{a \cdot d}{b \cdot c}$$

$$\psi_c = \frac{(a + 0.5) \cdot (d + 0.5)}{(b + 0.5) \cdot (c + 0.5)}$$

$$\lambda = \frac{p_e \cdot (R - 1)}{1 + p_e \cdot (R - 1)} \quad , \quad R = \psi_c$$

Figure 4. Relative odds (ψ), corrected relative odds (ψ_c), relative risk (R) and population-attributable risk (λ) of disease in hypertensives vs. non-hypertensives; **a**, **b**, **c** and **d** indicate numbers: p_e indicates the prevalence of hypertension in the population.

4.2 Prospective studies

4.2.1 Ten-year study of pensioners born in 1902 and 1903 (paper III)

Study groups

In 1969 and 1970 respectively, an extensive study was started on all pensioners born in 1902 and 1903 and living in the Dalby primary care district. The patient material consisted of 156 pensioners, or 82 % of the target population. They have undergone follow-up examinations every second year since then. Of these 156 pensioners, 144 reached the age of 70 years in 1972-73. The latter group comprised our cohort of pensioners used for a ten-year prospective study from 1972-73 (for details, see paper III, Fig. 2).

The cohort was dichotomized into those who had established hypertension at the age of 70 years ($n = 39$) and those who had not ($n = 105$). These groups were used for comparison of survival rates and the occurrence of myocardial infarction, stroke, symptomatic heart disease and diabetes. The medical

examinations performed in this study have been described elsewhere (48). Information about morbidity and mortality was obtained from the Health Centre, Lund University Hospital, other hospitals, private practitioners, autopsy reports and death certificates. The 34 pensioners not attending the first examination (non-attenders) were followed up by studying their medical records, autopsy reports and death certificates.

Epidemiological considerations

This study comprised 342 person-years in the hypertensive group and 889 person-years in the other group. The incidence rates and mortality rates were calculated in this study as well as the relative risks and attributable risks. This may be compared with the retrospective studies (including the case-control studies) where the relative odds (risk) only could be estimated.

The number of pensioners was small in this study. However, it comprised the entire group of pensioners born in 1902-03 in the primary care district who attained the age of 70 years.

4.2.2 Thirteen-year study of the prognostic value of a 'casual' blood pressure (paper VI)

Study group

The subjects were derived from a general ophthalmic population survey at the Dalby Health Centre covering from March 1969 to April 1970. Invitations with an appointment notification and a brief questionnaire were mailed in rotation, using a directory, to all persons aged 8 years or more, who had been residents of the village surrounding the Health Centre since December 1968. The fact that a measurement of the blood pressure was part of the examination was not mentioned in the invitation. The questionnaire included one question regarding medications currently being used.

Of 954 males invited, 828 (87 %) took part in the survey. Twenty-two men using drugs listed in the Swedish Pharmacopoeia of 1969 under the heading "Agents in Hypertension" were excluded from the present study, since we regarded their blood pressures as 'artificially' depressed and not representative of their 'true' blood pressures. For various reasons blood pressures were not measured in 13 males; hence the study group totalled 793 males (83 %). The attendance was high (over 80 %) even among those aged 80 years and more.

Information about deaths was obtained continuously from the Dalby Parish Office which has the primary responsibility for the census register in Dalby, as well as from the National Central Bureau of Statistics. It was based on necropsy (64 %) and death certificates (36 %).

Non-attenders

The death rates among the male non-attenders were compared with those of the attenders. In the age group 40-69 years the non-attenders showed a death risk of 2.2 (SE 0.9) vis-à-vis the attenders. In those aged 40-99 years the corresponding figure was 1.9 (SE 0.5).

Excluded probands

Of 22 males excluded because of antihypertensive drug treatment, 16 died during the observation period, 8 from a CCVD. All but 5 died after reaching the age of 70 years. The death rates among the excluded probands were compared with those of the included. In the age group 40-69 years the excluded showed a death risk of 4.7 (SE 2.3) vis-à-vis the included. In those aged 40-99 years the corresponding figure was 2.1 (SE 0.6).

Statistical and epidemiological considerations

In order to study the influence of blood pressure level on mortality, a regression analysis of blood pressure on age was first performed; the reason for this was that we deemed it necessary to relate the blood pressure measurement actually obtained from a proband to the "normal" blood pressure for a man of that age. As it is known that blood pressure increases with age, isotonic regression was considered a more adequate method than using either one or more single regression lines or a higher degree polynomial. Isotonic regression is a method which amounts to finding that increasing function which in the least-squares sense best approximates the points in the data set, as described by Barlow et al. (49). Such a regression, which is necessarily performed on a computer, produces a function which is not expressed by any explicit formula but rather in the form of a table or a graph (cf. Figures 5 and 6). In order to form each proband's **absolute excess pressure** (positive or negative), the difference between his actual recording and the value predicted by the regression curve was calculated.

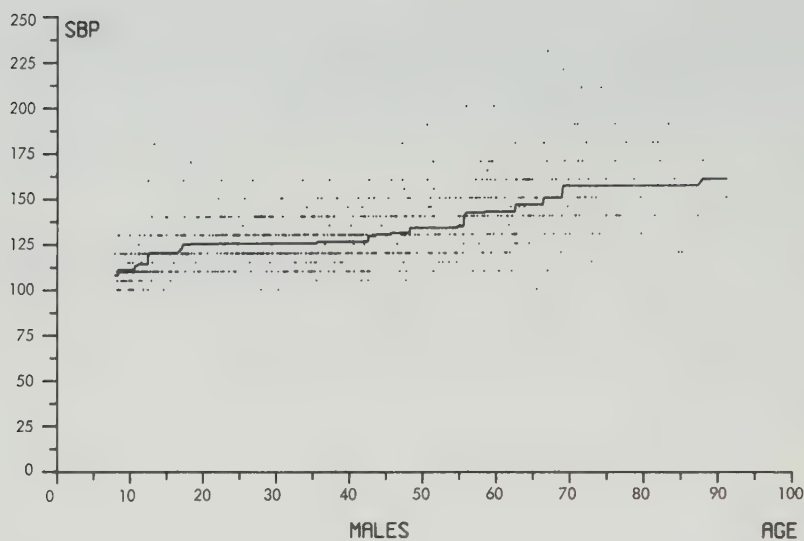


Figure 5. Recorded systolic blood pressures and their isotonic regression on age in 793 males.

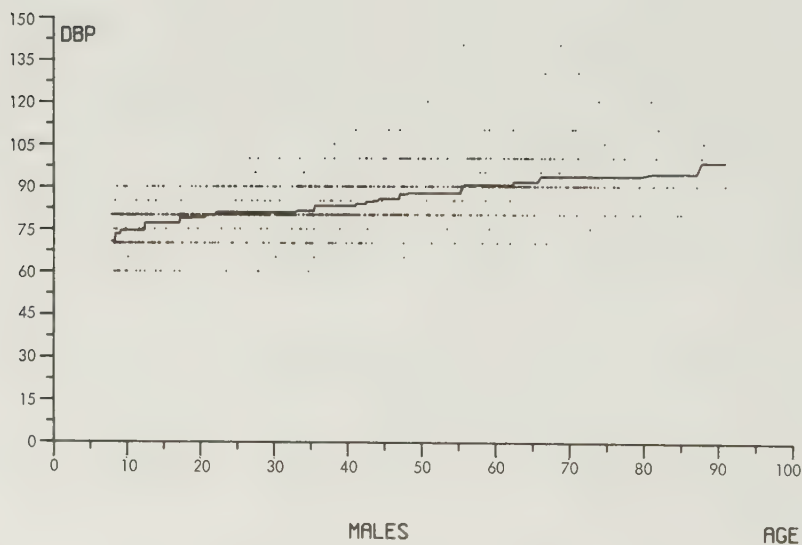


Figure 6. Recorded diastolic blood pressures and their isotonic regression on age in 793 males.

The individuals were then ranked according to their excess pressures and divided into quintiles. The first quintile (low-pressure group) and the fifth quintile (high-pressure group) were both compared with a third group (medium-pressure group) formed by the three medium quintiles. When two persons had equal excess pressures the older one was considered to have the lower excess pressure.

As the variation in blood pressure is usually greater at higher ages, the method used might produce more older persons in the extreme groups than in the medium one. To circumvent this, the normal variation $\sigma(a)$ at age a was estimated - in fact by using isotonic regression of the absolute residuals on age -, and the absolute excess pressure was standardized by dividing it by $\sigma(a)$; the quantity so obtained was called a **standardized excess pressure**. Both quantities described - absolute and standardized excess pressure - have been used in the analyses.

The number of person years at risk and the observed number of deaths were calculated for each of the three blood pressure groups and within each 5-year age interval. Indirect standardization was performed, using death rates for Malmöhus County minus Greater Malmö Area, in order to compensate for possible differences in age structure between the blood pressure groups. Thus, first a standardized mortality ratio and then a standardized death rate were obtained for each group.

The standardized death rates of the low and high blood pressure groups were divided by that of the medium one, giving an age-adjusted mortality ratio relative to that group. When some of the calculations were repeated using one-year age intervals instead of 5-year intervals the differences were negligible. The calculations described for overall mortality regarding absolute excess pressure were also performed for mortality in CCVD.

In order to separate early and late deaths in the low blood pressure group, analyses were performed separately for the first and the second half of the 13-year observation period.

Statistical significance was assessed, concerning death rates and mortality ratios, using two-sided tests and normal approximation, assuming Poisson variation among deaths observed. The Chi-square test was used to test the difference between frequencies in the two groups. The Yates correction for continuity was used when any of the expected frequencies was less than five.

Our ways of estimating and comparing mortality in the different groups are the standard ones. However, the technique of defining our groups is new, to the best of our knowledge; in particular we have found the use of isotonic regression advantageous: even if we do not claim that isotonic regression is an indispensable tool, we do contend that it simplifies the analyses and relieves the physician and the statistician from troublesome decisions such as choice of polynomial degree, choice of interval end points for age grouping, choice of whether or not a piecewise linear regression function should be continuous or not.

A disadvantage with isotonic regression, however, is that it presupposes the variable under study (in our case the blood pressure) to be monotonically increasing or, at worst, constant. In our material there was in fact a slight decrease in mean blood pressure in the highest age group (73 years and above; $n=29$) which we disregarded.

In our opinion, the technique used in this study is particularly relevant in connection with moderately sized materials like ours.

5. RESULTS AND DISCUSSION

5.1 Prevalence of hypertension and borderline hypertension (papers II, III and IV)

The prevalence of hypertension (both sexes) was estimated from the **control material** as described above to at least 4.4 % in the age group 40-49 years, 14.8 % in the age group 50-59 years and 18.8 % of those aged 60-69 years. The corresponding figures for borderline hypertension were 11.4, 12.5 and 13.6 %.

Most hypertensives were diagnosed before the examination: 100 % in the age group 40-49 years, 80 % in the age group 50-59 years and 92 % in those aged 60-69 years. Few borderline hypertensives had been diagnosed previously, 25 % in the age group 40-49 years, 19 % in the age group 50-59 years and 37 % in those aged 60-69 years.

Comment

Between 80 and 100 % of the hypertensives were diagnosed before the examination, thus indicating a good control of actual hypertension with the criteria for diagnosis described above. This may be a result of our effort to screen for hypertension among patients consulting the Health Centre.

However, only between 19 and 37 % of the patients with borderline hypertension were diagnosed before the examination. In the light of the results of recent studies regarding the benefit of treatment of mild hypertension (13-19) we must conclude that we are faced with a major problem which merits further studies regarding screening, treatment and follow-up of this group of patients in our primary care district.

5.2 Attainment of treatment objectives (papers II and III)

In the age groups 40-59 and 60-69 years the proportion of hypertensives who attained their treatment objectives amounted to about 75 %. In the calculation of these results the higher of the patients' two blood pressure recordings was compared with the treatment objective for both systolic and diastolic blood pressure.

In males in the age group 40-59 years an analysis was also performed using the last blood pressure values registered in the patients' medical records before the examination in 1981. The proportion of hypertensives who attained their treatment objective in this analysis was unchanged, viz. 75 %.

The hypertensives' blood pressure values were reduced by 33-40/19-24 mm Hg in comparison with the pre-treatment values. However, the patients' values were still about 16-21/9-11 mm Hg higher than those of the controls (for details, see paper II, Table II and paper III, Table I).

Comment

The hypertensives' blood pressure was reduced in accordance with what has been internationally accepted and 75 % attained their treatment objective. Thus, we regarded our patients' blood pressure as well treated. Our results may be compared with other and earlier studies where only about one-fourth of the hypertensives were adequately treated (50-51).

5.3 Life style parameters (papers II-V)

All patients and controls in the retrospective studies were asked about their smoking and alcohol habits. Male patients with myocardial infarction were also categorized as smokers or non-smokers at the time of admission to hospital. Patients and controls in the retrospective studies had measurements taken of their weight and height. Serum cholesterol and serum-triglycerides were not analysed in our studies.

5.3.1 Smoking (papers II, III and V)

The smoking habits differed between hypertensives and controls in males aged 40-59 years (paper II) but not in females (Table I). There were more ex-smokers among these male patients than among their controls and there was also a strong trend towards fewer smokers. In the age group 60-69 years (paper III) there was only a trend towards more ex-smokers and fewer smokers among the male hypertensives than among their controls (Table I). In females, however, there were fewer smokers and more non-smokers among the hypertensives.

The partial correlation coefficient between blood pressure group and smoking was -0.13 ($p = 0.05$) in males aged 40-59 years and 0.03 (N.S.) in females.

Among male patients with a myocardial infarction, 64 % were smokers at the time of admission to hospital (paper V) in comparison with 34 % of their controls.

Table I. Frequency of smoking in retrospective studies on hypertensives (Ht) and controls (C) aged 40-69 years; p indicates the level of significance (normal deviate test).

	Frequencies (%)					
	40-59 years			60-69 years		
	Ht	C	p	Ht	C	p
<u>Male</u>	(n=66)	(n=75)		(n=59)	(n=69)	
Smokers	21	36	0.05	30	36	N.S.
Ex-smokers	47	31	< 0.05	51	42	N.S.
Non-smokers	32	33	N.S.	19	22	N.S.
<u>Female</u>	(n=55)	(n=63)		(n=65)	(n=55)	
Smokers	20	25	N.S.	3	18	< 0.01
Ex-smokers	13	14	N.S.	9	11	N.S.
Non-smokers	67	60	N.S.	88	71	< 0.05

Comment

There were more ex-smokers and fewer smokers among the male hypertensives aged 40-59 years than among their controls. This may be attributable to advice given in the consulting room and thus indicates good treatment. However, we cannot disregard public opinion against smoking which may have affected the hypertensives more than the controls.

The high frequency of smokers among the patients with myocardial infarction (64 %) is striking and a well known risk indicator of this disease (52-55).

5.3.2 Alcohol (papers II and III)

The admitted alcohol habits did not differ between hypertensives and controls. Nor did the calculated alcohol consumption the week before the examination. However, levels of S-GT serum alanine aminotransferase (S-ALAT, $\mu\text{Kat/l}$) and serum aspartate aminotransferase (S-ASAT, $\mu\text{kat/l}$) were both higher in the hypertensives than in their controls in the age group 40-59 years. This was not the case in those aged 60-69 years.

The partial correlation coefficients between blood pressure group and alcohol habits were 0.05 (N.S.) in males aged 40-59 years and -0.20 ($p < 0.01$) in females. The coefficients between blood pressure group and S-GT were 0.07 (N.S.) in males and 0.20 ($p < 0.01$) in females.

Comment

The reliability of a structured interview in obtaining information about drinking habits has been analysed (56) and it was concluded that the frequency of drinking was satisfactorily self-reported, whereas reporting on the actual quantities of alcoholic beverages consumed was moderately reliable for non-alcoholics but unreliable for alcoholics. In our studies, hypertensives and controls were interviewed by the same nurse and in the same manner, concerning drinking habits. The hypertensives aged 40-59 years had higher S-GT, S-ASAT and S-ALAT values than had their controls. These findings tally with results published from other investigations (57-58).

Studies on age cohorts of middle-aged males in Malmö, the third largest city in Sweden, have shown correlations between S-GT and blood pressure indices (59). There were 38 % abnormal S-GT values ($> 1.1 \mu\text{kat/l}$) among hypertensives referred to the hypertension clinic in Malmö, in comparison with 18.5 % among the whole population under study (58). In the present studies, only 20 % of the male hypertensives aged 40-59 years had S-GT values $\geq 1.1 \mu\text{kat/l}$, vis-à-vis 10 % of the controls. These results may be explained by the differences in alcohol habits between inhabitants of a large city such as Malmö and a suburban area like Dalby, since S-GT may be regarded as an indicator of alcohol complication.

5.3.3 Obesity (paper II-IV)

Hypertensives of both sexes had higher body mass index than their controls in the age group 40-59 years as well as in those aged 60-69 years. The figures were: in males 28.4 vs. 25.0 and 28.0 vs. 25.4 respectively and in females 28.1 vs. 25.2 and 29.5 vs. 26.7 respectively.

The odds ratio of hypertension in males aged 40-59 years was estimated to 5.4 (95 % confidence interval 2.6-11.2) and in females to 2.5 (1.2-5.3.)

Comment

Hypertension and obesity are two common and interrelated health hazards (60). Hypertension is known to be more common in the obese, than among the non-obese. Conversely a significant proportion of hypertensives in a population are overweight (61-62). Obesity was shown in our studies to be an indicator of excess risk of hypertension, which ought to be remembered when screening for this disease. This may be compared with the Framingham study (61) where the risk of hypertension in previously normotensive individuals was proportional to the degree of overweight. This has also been confirmed in studies comprising more than a million people (63). It is therefore interesting to note that studies on limited numbers of cases and controls in a defined population in primary health care give results which are comparable to studies made on large populations.

5.4 Family history (paper IV)

The relative odds (risk) of hypertension in males aged 40-59 years with obese and hypertensive mothers was estimated to 8.0 (2.1-30.6) and in males with obese and hypertensive fathers to 6.1 (1.3-27.9). The corresponding figures in females were 4.4 (1.3-14.3) and 2.6 (0.3-23.6), respectively. There was no significant excess risk in males or in females with hypertensive but non-obese parents, although there was a trend in the same direction.

There was a significant excess risk of hypertension in males and females in this age group with hypertensive siblings as well as in males with a positive family history of myocardial infarction in fathers or in siblings (for details, see paper IV, Tables I-IV).

About 42 % of the male and 44 % of the female hypertensives in this age group reported maternal hypertension, in comparison with 12 and 22 % respectively of the controls. Paternal hypertension was reported by 25 % of the male and 21 % of the female patients, in comparison with 3 and 8 % respectively of the controls.

Comment

We have shown that a combination of obesity and hypertension in the parents tallies with a significant excess risk in their offspring. This was not so in those with parental hypertension without obesity. To avoid a type II fallacy it should be emphasized that this difference between the groups may be explained by the limited numbers in our study. However, although all results point in the same direction (excess risk) three of four reach significance in the former group whereas no results reach significance in the latter. This indicates that parental hypertension together with obesity is a stronger risk indicator of hypertension in offspring than is parental hypertension in itself. Studies in adolescents have shown that familial blood pressure resemblances are not explained solely by familial similarities in body weight (64). There was a high degree of validity of the estimates of parental obesity in our study, as shown in Figure 1.

A positive family history of hypertension is an established risk indicator of this disorder (65-66). Our results compare well with studies on middle-aged males in Malmö (67) where maternal hypertension was also twice as common as the paternal.

In our study, the family history of hypertension was categorized as "positive" only if a person claimed a first-degree relative to have consulted a doctor or a nurse because of high blood pressure. Otherwise, it was categorized as "negative" or "uncertain". There was no significant difference between the groups regarding frequencies of "uncertain" answers. The patients may be more aware of cardiovascular diseases and hypertension in their relatives, since they are hypertensives themselves, in contrast to the controls who are mostly healthy. It has been found, however, that middle-aged males' knowledge of their parents' diseases and cause of death is reliable and can be used for therapeutic purposes in familial disease (68).

In this study a positive family history of stroke was not found to be a significant risk indicator of stroke. However, this may be due to the limited numbers. Others have shown that middle-aged men with a cardiovascular risk profile have parents and siblings with increased cerebro-cardiovascular morbidity and mortality (69).

Our studies point out three risk indicators of hypertension: obesity (as discussed under 5.3.3), parental obesity combined with hypertension, and a positive family history of myocardial infarction. How these findings can be utilized in the diagnosis of unknown hypertension in a primary care district, and whether they have any bearing upon borderline hypertension, merit further studies.

5.5 Risks of cerebro-cardiovascular morbidity and mortality

5.5.1 Morbidity in hypertensives below the age of 70 years (papers II, III and V)

The frequencies of CCVD and diabetes in hypertensives aged 40-59 and 60-69 years in comparison with controls are shown in Tables II and III, respectively.

Table II. Frequencies (%) of cerebro-cardiovascular diseases (CCVD) in hypertensives (Ht) aged 40-59 years, in comparison with controls (C); p indicates the level of significance (chi sq test).

	Frequencies (%)		
	Ht	C	p
<u>Male</u>	(n=66)	(n=75)	
CCVD	21	1	< 0.001
- stroke	2	0	N.S.
- coronary heart disease	20	1	< 0.001
- claudicatio	2	0	N.S.
Diabetes	8	5	N.S.
<u>Female</u>	(n=55)	(n=63)	
CCVD	8	0	N.S. ¹
- stroke	4	0	N.S.
- coronary heart disease	2	0	N.S.
- claudicatio	2	0	N.S.
Diabetes	5	2	N.S.

¹ = chi sq (corrected) 2.7, N.S. chi sq (raw) 4.8, p < 0.05

Table III. Frequencies (%) of cerebro-cardiovascular diseases (CCVD) in hypertensives (Ht) aged 60-69 years, in comparison with controls (C); p indicates the level of significance (chi sq test).

	Frequencies (%)		
	Ht	C	p
<u>Male</u>	(n=58)	(n=69)	
CCVD	36	12	< 0.01
- stroke	14	1	< 0.05 ¹
- symptomatic heart disease	12	6	N.S.
- myocardial infarction	17	7	N.S.
Diabetes	16	6	N.S.
<u>Female</u>	(n=64)	(n=55)	
CCVD	14	7	N.S.
- stroke	2	2	N.S.
- symptomatic heart disease	11	2	N.S. ²
- myocardial infarction	3	2	N.S.
Diabetes	11	4	N.S.

¹ = chi sq (corrected) 5.5, p < 0.05; chi sq (raw) 7.3 , p < 0.01

² = chi sq (corrected) 2.6, N.S.; chi sq (raw) 3.92, p < 0.05

CCVD were more common in male hypertensives than in their controls. In females there was a trend in the same direction which did not reach significance.

The relative odds (risk), corrected for small numbers, of CCVD was estimated to 13.7 (2.5 - 76.7) in male hypertensives aged 40-59 years, as shown in Figure 1. The odds in those aged 60-69 years was 4.3 (1.7-10.1).

During the period 1973-82 there were 91 cases of myocardial infarction in males born between 1912 and 1931 and living in the Dalby primary care district. The corresponding figure for females was 20. There were 51 cases of stroke in males and 20 in females.

The relative odds, corrected for small numbers, of myocardial infarction in **hypertensive males** was estimated to 3.8 (1.8-8.0) as illustrated in Figure 4. When the estimates were calculated for smokers and non-smokers separately the odds of hypertension was higher in smoking males than in non-smokers, 4.9 (1.6-15.2) and 2.2 (0.8-6.4) respectively.

The relative odds, corrected for small numbers, of myocardial infarction in **smoking males** was estimated to 3.3 (1.7-6.2). When the estimates were calculated for hypertensives and non-hypertensives separately the odds of smoking was higher in the hypertensive males than in non-hypertensives, 5.3 (1.4-20.5) and 2.4 (1.1-5.1) respectively.

The population-attributable risk of hypertension with respect to myocardial infarction in males was estimated to 30 % in all males, 37 % in smokers and 15 % in non-smokers.

The relative odds, corrected for small numbers, of stroke in **hypertensive males** was estimated to 12.3 (4.3-35.5). The population attributable risk was estimated to 63 %.

As there were few female cases, we have analysed myocardial infarction and stroke combined as CCVD. The relative odds, corrected for small numbers, of CCVD in **hypertensive females** was estimated to 2.1 (0.7-5.9); Chi sq was 2.0, N.S. The population-attributable risk was not estimated.

Comment

This study has shown that a limited number of patients in a defined population can be utilized in epidemiological studies regarding risk and may therefore justify this model for studies in primary health care.

Our results show that male hypertensives run a high risk of developing CCVD even when their blood pressure has been reduced in accordance with internationally accepted values. However, their values were still 16-21/9-11 mm Hg higher than those of their age- and sex-matched controls.

Two-thirds of the middle-aged male hypertensives with CCVD had their hypertension diagnosed before, and one-third at the time of the complication(s). We found no differences in the proportions of patients who attained their treatment objectives at the examination when hypertensives with vs. without CCVD were compared ($\chi^2 = 0$) nor did their blood pressure values before treatment differ. However, this analysis does not consider adherence to treatment objectives during the period between the start of treatment and the present examinations.

In females there was only a trend towards more CCVD, which did not reach significance, when hypertensives were compared with their controls. To avoid a type II fallacy it should be emphasized that this may be explained by the limited numbers, and does not indicate that hypertension is unassociated with CCVD in women.

During a ten-year period there were 20 females and 91 male patients born between 1912 and 1931 who suffered myocardial infarction in the Dalby district. The corresponding figures for stroke were 20 and 51. The Framingham study showed women to tolerate hypertension no better than men with respect to cerebrovascular disease (70) but for coronary heart disease the risk in females was about half of that in men (71). Bechgaard showed hypertensive women to have lower mortality than men of the same age and blood pressure group (72). In a 12-year follow-up of middle-aged women in Gothenburg the incidences of myocardial infarction, stroke and overall mortality were no higher than expected in hypertensive females offered continuous medical care (73,74).

The excess risks of myocardial infarction and stroke in males confirm our earlier retrospective studies on CCVD in hypertensives vs. non-hypertensive controls. The population-attributable risk of hypertension in the population with regard to myocardial infarction and stroke in males was estimated to 30 and 63 % respectively. This risk was higher in smoking (37 %) than in non-smoking (15 %) hypertensives with regard to myocardial infarction. The concept of population-attributable risk is useful in that it provides an estimate of the amount by which myocardial infarction and stroke might be reduced in the population if hypertension could be removed.

Our figures are in agreement with results obtained in large prospective studies (52,70-72). In the Framingham study, hypertension was the most common precursor of atherothrombotic brain infarction. The risk of brain infarction in that study was about four times as high in hypertensives as in normotensives.

The corresponding risk of ischaemic heart disease was about twice as high. Our results may also be compared with the 1979 Build and Blood Pressure Study (75) comparing four million non-hypertensive and 26,000 hypertensive insurance policy holders in U.S.A. The **mortality** ratio in treated hypertensives with systolic blood pressure in the group with 148-157 mm Hg was 170 vis-à-vis 111 in the group with 128-137 mm Hg. Our middle-aged hypertensives had a systolic blood pressure value during treatment of about 149 vis-à-vis 133 mm Hg in their controls (paper II). A further blood pressure reduction in our patients may be achieved with intensified drug therapy, which however, may lead to an increase in adverse effects (76) and may seriously disturb the patients' quality of life and interfere with their compliance. A reduction of this magnitude may be accomplished by weight reduction and probably by intervention in factors linked to obesity (77-79). This may be one way to reduce the excess risk in male hypertensives. However, it will necessitate documentation through further studies.

5.5.2 Morbidity and mortality in hypertensives aged 70 years and above

No significant differences were found in mortality (Fig. 7) or in cardiovascular morbidity (Table IV) between the hypertensive and the non-hypertensive subcohorts. The relative risk of death for the hypertensives was 0.7 (0.3-1.4). Necropsy (80 %) and death certificates (20 %) did not reveal any differences in mortality when the non-attenders were compared with the two subcohorts.

The hypertensive pensioners at the age of 70 years had significantly higher blood pressure values - systolic and diastolic - than the non-hypertensives, although about two-thirds of the former received antihypertensive drug treatment.

Comment

Our results did not show any significant excess risk of morbidity or of mortality in the hypertensive subcohort, in comparison with the non-hypertensive. In fact, the relative risk of death was 0.7 for the hypertensives. The numbers were small in this study but comprised all pensioners born in 1902-03 in the district who attained the age of 70 years. To avoid a type II fallacy it should be emphasized that a significant difference between the groups may exist which might have emerged if the numbers had been larger.

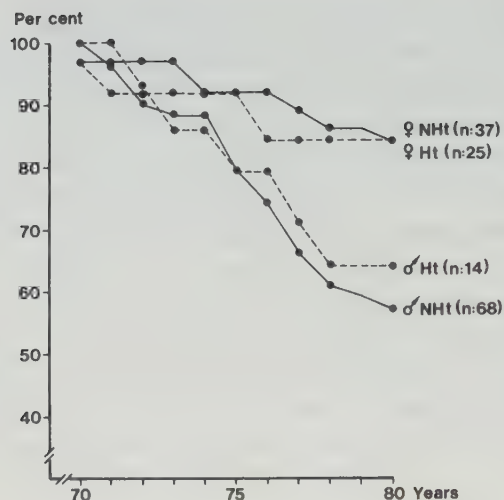


Figure 7. Survival rates of male and female pensioners born in 1902-03 who reached the age of 70 years and had a diagnosis of hypertension (Ht), in comparison with pensioners without hypertension at that age (NHt).

Few studies have reported on morbidity and mortality in pensioners aged 70-80 years. Fry (80) found in a study of the natural history of hypertension (DBP $\geq$ 100 mm Hg) an observed/expected death ratio in untreated hypertensives of 1.15 in the age group 60-69 years and of 0.87 in those aged 70 years and above. His conclusion was that the risk to life with high blood pressure varies with the age at which hypertension is first observed, and that above the age of 60 years there seems to be no extra risk of death for (untreated) hypertensives. That study was performed in a suburban area of London comprising patients from Fry's general practice. Our prospective study of (treated) hypertensives aged 70-80 years comprising all pensioners in the district who attained the age of 70 years shows results similar to Fry's.

Andersson & Cowan (81) showed that neither systolic nor diastolic blood pressure had any predictive value for survival in healthy pensioners aged 70-89 years attending a health centre for old people. These pensioners did not, however, represent a random sample of the population, as the centre was an experiment designed to provide clinical facilities for the early detection of disease in the elderly and intake was dependent on general practitioners' referral.

Table IV. Ten-year incidence rates of CCVD and diabetes in a cohort of pensioners born in 1902 and 1903 dichotomized into those with hypertension (Ht) and those without (NHt) at the age of 70 years.

Disease group		Incidence rate per 1000 person-years	Relative risk	Attributable risk per 1000 person-years
Stroke	NHt	12.4	1	8.1
	Ht	20.5	1.7	
Symptomatic heart disease	NHt	29.2	1	5.9
	Ht	35.1	1.2	
Myocardial infarction	NHt	16.9	1	6.5
	Ht	23.4	1.4	
Diabetes	NHt	6.8	1	2.0
	Ht	8.8	1.3	

Agner (82) showed in a ten-year population study of men and women aged 70 years that high systolic blood pressure at the age of 70 had an independent predictive value for excess cerebro-cardiovascular as well as overall mortality in women but not in men. High diastolic pressure had no independent predictive value in either sex. However, high systolic blood pressure had an independent predictive value for excess cerebro-cardiovascular morbidity in both sexes.

In the Framingham study (83) subjects of both sexes between 65 and 74 years with hypertension had an annual incidence of CCVD three times as great as in normotensive persons.

The EWPHE study (European Working Party on High Blood Pressure in the Elderly) which is specially designed to evaluate the potential benefits of anti-hypertensive treatment (84) has not yet reported its findings regarding morbidity and mortality in elderly patients on active treatment compared with placebo.

In our investigations we found an excess risk of CCVD in hypertensives aged 60-69 years, but not in those aged 70-80 years. This difference could be influenced by the design, which compared a retrospective with a prospective study. However, the difference can be attributed to a selection process, with greater survival and less morbidity among those in a population who reach the age of 70 years. In the light of these results we conclude that further investigations are needed, especially among elderly hypertensives, concerning the benefits of drug treatment.

5.5.3 Mortality risk in the population as indicated by a 'casual' blood pressure

Of 793 men examined in 1969-70, 89 died during the 13-year observation period (11.2 %): 84 in the age group 40-99 years and 29 in the age group 40-69 years. The corresponding figures for deaths from CCVD were 45, 44 and 14, respectively.

Men in both extreme blood pressure quintiles showed an excess death risk in comparison with those of the medium group, as can be seen in Table V and Figure 8. This was so regardless of whether absolute or standardized excess blood pressure was analysed and regardless of whether systolic or diastolic pressure was considered. The mortality ratios were higher in the age group 40-69 years than in the age group 40-99 years.

The death risk in the low blood pressure group relative to the medium one in age group 40-69 years was 3.5 (SE 2.1) when computed for the first half of the observation period and 1.6 (SE 1.0) for the second half. The corresponding figures for the high blood pressure group relative to the medium one were 2.9 (SE 1.9) and 0.9 (SE 0.7), respectively. The figures were lower but the trend similar although less pronounced when we analysed the entire age group 40-99 years.

Comment

Men in both extreme groups showed an excess death risk in comparison with those of the medium group; thus, mortality was a U-shaped function of excess blood pressure (as defined above). The study comprised deaths in men from the age of 40 years who were observed over a 13-year period. There were few deaths and comparisons of death risks did not reach statistical significance at the 5 % level. However, all comparisons in the age group 40-69 years and most in the group 40-99 years pointed in the same direction, thus supporting a very strong trend.

Table V. Death rates per 10 000 person years (p.y.) for males aged 40-69 and 40-99 years with low, medium and high absolute excess blood pressure (AEBP) and standardized excess blood pressure (SEBP) and mortality ratios relative to the medium blood pressure group.

	40 - 69 years		40 - 99 years	
	Death rate per 10 000 p.y. (SE)	Mortality ratio (SE)	Death rate per 10 000 p.y. (SE)	Mortality ratio (SE)
Systolic AEBP				
Low	135 (37)	2.9 (1.3)	239 (44)	1.4 (0.4)
Medium	46 (15)	-	167 (30)	-
High	89 (34)	1.9 (1.0)	250 (50)	1.5 (0.4)
Systolic SEBP				
Low	131 (42)	2.4 (1.0)	236 (57)	1.2 (0.3)
Medium	55 (16)	-	196 (28)	-
High	95 (36)	1.7 (0.8)	223 (51)	1.1 (0.3)
Diastolic AEBP				
Low	120 (38)	2.3 (1.0)	258 (59)	1.5 (0.4)
Medium	53 (16)	-	171 (25)	-
High	102 (36)	1.9 (0.9)	313 (70)	1.8 (0.5)
Diastolic SEBP				
Low	128 (40)	2.5 (1.1)	265 (61)	1.6 (0.4)
Medium	51 (15)	-	168 (25)	-
High	106 (37)	2.1 (1.0)	319 (71)	1.9 (0.5)

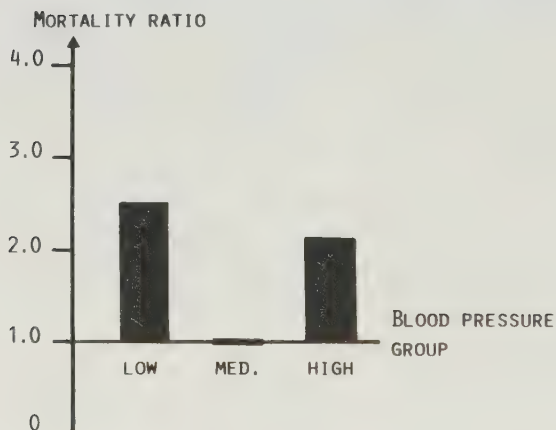
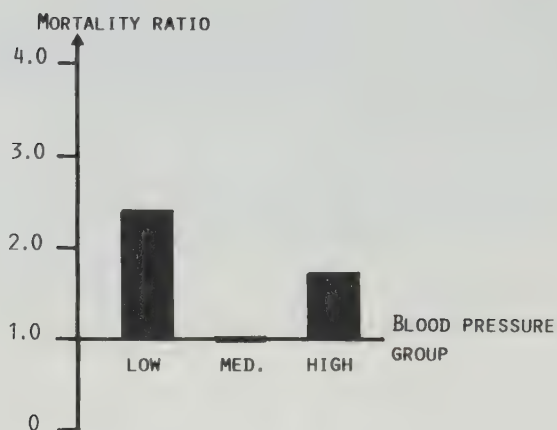


Figure 8. Mortality ratios (total deaths, 13-year follow-up) in ages 40-69 years of low and high blood pressure groups relative to the medium group; systolic standardized excess pressure (above) and diastolic standardized excess pressure (below).

The most interesting finding of our study was the high death rate among men in the **low** blood pressure group in comparison with the medium one (Table V). When the calculations were performed separately for the first and the second half of the observation period, the mortality ratio of the low pressure group vis-à-vis the medium one was higher during the first half. In other words, there were more early deaths than late ones in the low blood pressure group, thus indicating an inhomogeneity in this group. When the medical records of the deceased were extracted and studied (Table VI), 71 % of the dead men in the low pressure group had suffered from a chronic disease (CCVD, chronic bronchitis, or malignant neoplasm) at the time of the examination, in comparison with 21 % of those in the medium group. Almost half of the dead men in the low pressure group had suffered from a CCVD before the examination. These results tally with the high early death rate in the low pressure group.

In the **high** blood pressure group there was also an excess death risk when compared with the medium group. This difference was explained by deaths during the first half of the observation period, thus suggesting an inhomogeneity in the former group; however, examination of the records provided no further insight (Table VI).

The over-mortality in our high pressure group accords with the Framingham (85) and other studies (52,75,86). The Framingham study, however, did not show any U-shaped mortality curve. This may be explained by the fact that persons with CCVD at entry were excluded from that study which furthermore only comprised two-thirds of the random sample invited. In the Bergen study (87) the age-specific total death rate in men showed a general increase with increasing systolic blood pressure, while the corresponding curve for diastolic blood pressure was more U-shaped. The curves were distinctly U-shaped in women in the Bergen study.

In prospective studies on middle-aged women in Gothenburg (74) there was a tendency towards a U-shaped pattern for CCVD as a function of blood pressure. There was, however, no obvious U-shaped pattern regarding mortality in that study.

Table VI . Frequency (%) of chronic disease at the examination in those males who died aged 40-99 years (data available on 70 out of 84).

p indicates the level of significance, chi sq test.

	Frequency (%)					
	Low BP	Med BP	High BP	P		
	(n=24)	(n=24)	(n=22)			
	L	M	H	Lvs.M	Lvs.H	Mvs.H
Chronic disease	71	21	18	<0.001	<0.001	N.S.
- CCVD	46	8	18	<0.01	<0.05	N.S.
- Chronic bronchitis	29	12	9	N.S.	N.S.	N.S.
- Malignant neoplasm(s)	17	4	0	N.S.	N.S.	N.S.
No chronic disease	29	79	82			

Male patients receiving antihypertensive treatment were excluded from our study for reasons given above. If they had been included they might have influenced the results of the age group 40-99 years, but hardly those of the 40-69 year group.

Thus, when analysing overall mortality it is important to consider the characteristics of the population under study, since different risk factors may vary in importance to different subgroups.

6. GENERAL SUMMARY

Responsibility for the treatment of hypertensives in Sweden will in the future be the concern of the primary health services. It is therefore important that research into hypertension should also be carried out within primary health care in order to find new models and methods for screening, treatment and follow-up of hypertension, as well as to analyse the effects of our endeavours. In primary health care the number of people in each catchment district is limited. This necessitates the use of research models that can be applied to small groups of people and yet give valid results.

For more than a decade the Dalby population has been subjected to extensive studies regarding blood pressure as well as to an anti-hypertensive program, and data have been registered in both in-patient and out-patient computer schemes.

In the light of our earlier studies and in studying reports from other investigations we found it of interest to analyse the efficacy of our existing treatment and follow-up program for hypertensives.

Our investigation has shown:

- **that** our hypertensives above the age of 70 years had no significant excess risk of cerebro-cardiovascular disease (CCVD) or mortality and that therefore hypertension **may** differ as a risk indicator in elderly people above and below the age of 70 years;
- **that** our male hypertensives below the age of 70 years ran a high risk of developing CCVD even though their blood pressure values had been reduced in accordance with what has been internationally accepted and 75 % of them attained their treatment objectives;
- **that** the hypertensives' blood pressure values during treatment were still about 20/10 mm Hg higher than those of the controls;
- **that** the impact of hypertension on the male population with regard to myocardial infarction and stroke - the population-attributable risk - could be estimated to 30 and 63 %, respectively;
- **that** smoking and hypertension were independent risk indicators of myocardial infarction in men;

- **that** the smoking habits in the middle-aged male hypertensives had been favourably influenced, which may be an effect of our treatment program, thus indicating good treatment;
- **that** the alcohol consumption among the hypertensives was as high as among the controls even though advice to reduce it had been given to the patients; in fact, the S-GT values were higher in the middle-aged hypertensives than in the controls;
- **that** the hypertensives were more obese than their controls, even though the patients had been recommended a low-calorie and low-sodium diet;
- **that** obesity, hypertension in obese parents, hypertension in siblings and a positive family history of myocardial infarction were risk indicators of hypertension;
- **that** most hypertensives in the population were diagnosed prior to the investigation, thus indicating a good control of actual hypertension;
- **that** few patients with borderline hypertension had been diagnosed earlier, thus indicating a major problem which merits further studies regarding screening, treatment and follow-up of this group;
- **that** isotonic regression analysis of blood pressure on age was a suitable technique with which to define study groups for mortality analysis in a moderately sized population where blood pressure increases with age;
- **that** both high and low blood pressures in men were found to be risk indicators of death and that an inhomogeneity was likely in both the lowest and the highest blood pressure quintiles;
- **that** limited numbers of subjects in a defined population can be utilized in epidemiological studies regarding risk and thus justify our models for studies in primary health care.

7. CONCLUDING REMARKS

Our hypertensive subjects have been accorded considerable interest for almost 15 years and their blood pressure values have been regarded as adequately reduced. However, those who were below the age of 70 years, but not above, were found to run a high excess risk of developing CCVD, when compared with a control group free from hypertension, chosen from the same suburban district and matched for age, sex and race. This discouraging result gives rise to several questions which merit further studies in primary health care: Do we diagnose our hypertensives too late? Should we increase their therapy and reduce their blood pressure values to the level of the controls, even at the cost of causing side effects? Why have we not succeeded in reducing the patients' weight to anywhere near that of the controls? How can we reduce the patients' alcohol consumption below that of the controls? Should metabolic factors be considered in the prevention of CCVD, or should we tackle with quite other - non-biological - factors? Our discouraging results accord with other and larger studies, e.g. MRFIT (25) and the WHO cardio-preventive study (88).

Our study has also shown that hypertension in obese parents is a stronger risk indicator of hypertension in offspring than is parental hypertension itself. How this finding can be utilized in diagnosis of unknown hypertension in primary health care and whether it has any bearing upon borderline hypertension also merit further studies.

In our follow-up of 'casual' blood pressure values we found men in both extreme blood pressure quintiles to have an excess death risk in comparison with those in the medium group. Thus, mortality was found to be a U-shaped function of (excess) blood pressure. These differences were explained by deaths during the first half of the observation period in both extreme quintiles, suggesting an inhomogeneity in these groups. Thus, when analysing overall mortality it is important to consider the characteristics of the population being studied, since different risk factors may be important to different subgroups.

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8. ACKNOWLEDGEMENTS

I wish to express my sincere gratitude to all the following:

- Professor Bengt Scherstén, my supervisor and friend, who introduced me to the field of hypertension research and generously shared with me his deep knowledge, critical approach, enthusiasm and support;
- Assistant Professor Bo Bengtsson, for constant support, valuable advice and constructive criticism;
- Assistant Professor Thomas Thulin, for valuable advice and interest;
- Associate Professor Jan Lanke, for valuable statistical advice and for introducing me to isotonic regression analysis;
- Associate Professor Lena-Pia Lindholm, for generous advice in research methodology;
- Göran Ejlerstsson, for valuable statistical advice, especially concerning the out-patient computer scheme;
- Thor Lithman, for valuable advice concerning the in-patient computer scheme;
- Margareta Olsson, S.R.N., whose competent assistance made this study possible;
- Karin Svenninger, for generous and never-failing assistance in revising the manuscripts;
- Ingrid Jönsson, Regina Ringkvist, Inger Ekvall and Monica Pålsson, for generous and qualified secretarial assistance;
- Mary-Ann Bengtsson, for generous assistance concerning the follow-up of pensioners born in 1902 and 1903;
- Sven Svensson, for producing the figures skilfully;
- Lennart Månsby, Agneta Sternerup, Arne Sundström and Bo Zöger, for carrying out the data processing;
- Max Brandt for revising the English text;

- colleagues, nurses and inhabitants of the Dalby Primary Care District for making this study possible;
- my own family, - Lena-Pia, my wife, and our daughters Annika and Sara-Lotta, as well as my parents-in-law Barbro and Sven Hagman, who all gave me their warm support in every possible way during my work. Their interest and encouragement have been my greatest source of joy and stimulation.

Dalby in April 1984

Lars Lindholm

I

EFFICACY OF A DISTRICT NURSE PROGRAM IN FOLLOW-UP OF HYPERTENSIVES

A Two-year Single-group Study in a Swedish Primary Care District

by

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SUMMARY

A two-year single-group study in primary health care of 223 hypertensives with blood pressure under satisfactory control was performed to investigate whether the patients could be referred to district nurses for their follow-up between visits to district physicians, without risking loss of control over their blood pressure. The study comprised 275 person-years. The mean age was 63.0 ± 14.4 years.

The initial attendance rate at the nurses' was high (78-92 %) but the tendency to continue the follow-up was lower (36-51 %). Lack of information was the major reason for patients who discontinued the follow-up without acceptable reasons. Most non-attenders had concomitant chronic diseases and visited the health care centre because of these. About 90 % of all patients returned to the district physicians as scheduled. Most attenders maintained their goal of treatment during the study.

Hypertensives above the age of 50 years whose blood pressure is under satisfactory control and who do not require regular visits to the health care centre for other chronic diseases may be referred to district nurses for follow-up without risking loss of control over their blood pressure.

INTRODUCTION

Primary health care ought to be the basis for the long-term management and follow-up of patients with chronic diseases such as diabetes, hypertension and arthritis. In Sweden such care is provided by district physicians working in health care centres and by district nurses who work in surgeries often decentralized from the health care centres. For several years, special clinics run by doctor-and-nurse teams have been organized, first in hospitals and later also in health care centres, for the care and follow-up of diabetics (1) and hypertensives (2-5).

District nurses now seem to be taking on increasingly important duties both in the prevention and in the care of patients with chronic diseases.

Management programs with uniform guidelines for clinical work-up, treatment and follow-up of hypertensives have been put into effect in various parts of Sweden in order to make the care more effective (3,5). The basis for these programs has been worked out by the National Board of Health and Welfare (6) and other authorities.

In Dalby, a suburban area in southwest Sweden, a clinic for hypertensives has been organized within the Health Care Centre. It has been run by a specially trained nurse for ten years. In this clinic the nurse sees the hypertensives between visits to the district physicians. She records their blood pressure, instructs them regarding diet and medication, checks compliance and follows up laboratory tests according to the regional management program for hypertensives. About half of all known hypertensives in the area were registered at this clinic in 1981, while the remainder received regular care from the district physicians.

Hypertensives, however, often suffer with complex health problems having social aspects for which they consult a district nurse. The latter has her surgery near the patients' homes and is often well known to them.

The aim of this study was to investigate whether hypertensives above the age of 50 years and with blood pressure under satisfactory control could be referred to a district nurse for their follow-up between visits to the district physician, without risking loss of control over their blood pressure. The following questions were asked:

- Do the referred patients visit the district nurse as scheduled?
- Do the patients continue the follow-up throughout the observation period?
- Do the patients return to the district physician as scheduled?
- Do the patients keep their blood pressure equal to or below the treatment goal?

METHOD AND STUDY POPULATION

The study area

The Dalby primary care district is situated in southwest Sweden, in the county of Malmöhus. The district had about 20,500 inhabitants in January 1981. It consists of four villages (Dalby, Genarp, Veberöd and Sandby), each having a small surgery for district nurses. There was only one health care centre (Dalby) in the district in 1981 but a second one (Sandby) was opened in September 1982.

Study population

Altogether 229 patients were referred during the study (Fig. 1). Twenty-three months after the start, all forms were collected from the district nurses and the medical records at the health care centres were studied. In 223 cases - 144 female and 79 male - forms and medical records were found. In six cases, however, either the referral form or the medical record could not be found and these cases were therefore excluded. The mean age at the end of the study was 63.0 ± 14.4 (mean $\pm$ SD) years. Of all patients, 78 % had hypertension and 22 % borderline hypertension. In 43 % of the cases the patients were registered at the clinic for hypertension before the referral. Altogether 275 person-years were studied. The observation period (mean $\pm$ SD, months) was 15.8 ± 6.1 in Dalby, 16.7 ± 5.0 in Genarp and 16.0 ± 5.1 in Veberöd.

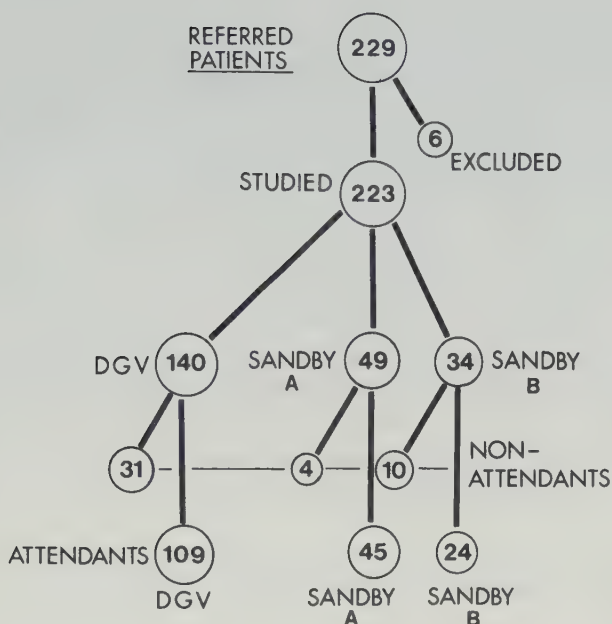


Figure 1. Hypertensives referred to district nurses for follow-up.
DGV = Dalby, Genarp and Veberöd areas.

Criteria for diagnosis of hypertension

The limits applied in the daily routine for non-symptomatic patients were (mean of three recordings) for hypertension $> 170 / > 105$ mm Hg (age group 40-59 years); $> 180 / > 110$ mm Hg (age group 60 years or more) and for borderline hypertension 160-170/95-105 mm Hg (age group 40-59 years); 170-180/105-110 mm Hg (age group 60 years or more). When a patient had diabetes, the limits were 5-10 mm Hg lower.

Goal of treatment

Our objectives for the treatment of hypertension in 1981 were: for the age group 40-59 years $\leq 160 / \leq 95$ mm Hg and for those aged 60 years or more $\leq 180 / \leq 100$ mm Hg. Each diabetic had an individually set goal, generally 5-10 mm Hg lower.

Organization

Hypertensives of both sexes aged 50 years or more and with blood pressure well under control (e.g. the objective of treatment was attained) were referred to the district nurses for follow-up examinations every third or fourth month - or earlier when indicated. The patients were instructed when to make a new appointment with the district physician - usually after one year.

A written instruction both for the district physicians and for the district nurses and a special form for referral were worked out and agreed upon. Information was given to the district nurses about the patient's name, age (civic registration number), address, telephone number, diagnoses, therapy, blood pressure at the latest recording, purpose of treatment, time of the next visit to the district nurse as well as to the district physician. The forms were mailed to the district nurses and were kept in a special file in their surgeries.

All district nurses were educated regarding hypertension and trained in blood pressure measurement technique and their surgeries were equipped with mercury manometers. These were checked regularly both by technicians and by the nurse specially trained in hypertension. Cuffs of different sizes (12 x 35 cm, 15 x 43 cm) were used, depending on the arm circumference (7).

All recordings were made with the patient in a recumbent position after five minutes of rest - if nothing else was indicated on the form. Diastolic blood pressures were phase V. Recordings were noted on the back of the form.

The district physicians were instructed how to refer the hypertensives and to note the purpose of treatment on all referral forms. They were also instructed to inform the patients carefully about the follow-up and, when indicated, to prescribe drugs to suffice until the next appointment.

Each patient was given a card on which blood pressure was noted. The patient was instructed to bring this card when visiting the district physicians.

At the end of the study the medical records of those patients who did not visit the district nurses were studied in all areas, except in Sandby (for reasons noted below). Their age and sex did not differ from those who attended.

Patients who at first visited the district nurse but then discontinued the follow-up without an acceptable reason in their medical records were invited to agree to a structured telephone interview. They were asked:

- 1) Were you referred to the district nurse for a follow-up of your blood pressure?
- 2) Were you informed by the district physician or by the district nurse about the planned intervals of the follow-up examinations?
- 3) Did you have any (special) reasons for discontinuing the follow-up at the district nurses'?
- 4) Were you informed when to return to the district physician?

The age and sex of these patients did not differ from the other cases in the same areas ($p > 0.05$).

A second health care centre (Sandby) was opened in the district about a year after the start of the study. In Sandby, district physicians and nurses work as a team, which alters the basis for the study in this area. The results from Sandby are therefore presented in two parts: cases referred before the new health care centre opened (Sandby A) and cases referred subsequently (Sandby B). The observation period, mean $\pm$ SD (months) was 17.1 ± 4.7 for Sandby A and 6.2 ± 2.5 for Sandby B.

Sandby B was not included in the statistical analyses in Tables I-II because of the new method of collaboration and the short observation period.

Statistical methods

Student's *t*-test was used to test the hypothesis of no difference in mean values between two groups. Chi-square test was used to test the hypothesis of no difference between frequencies.

The statistical significance was evaluated by two-tailed tests at the levels $p < 0.05$, $p < 0.01$ and $p < 0.001$. A difference was considered statistically significant when the *p*-value was < 0.05 .

RESULTS

As can be seen from Table I, Sandby A had a higher ($p < 0.05$) attendance rate than the Dalby, Genarp and Veberöd areas (DGV). These areas are presented as a single-group in Tables I and II, since there were no differences between them. Most of the patients appeared at the scheduled time in all areas.

Regarding the tendency of the patients to continue the follow-up at the district nurses' during the observation period (Table II), there were no significant differences between the areas (chi-square = 2.35, N.S.).

Fifteen and twenty per cent respectively in DGV and Sandby A failed to appear for follow-up without an acceptable reason noted in their medical records. A somewhat larger group discontinued with an acceptable reason (e.g. the physician terminated the follow-up as the blood pressure had risen above the limits or the patient had contracted some other disease), leaving only 36 and 51 % respectively continuing the follow-up at the district nurses'.

A blood pressure equal to or below the treatment objective was attained by 86 % of all attending hypertensives (Sandby B excluded) who had such an objective noted on their form ($n = 140$). The non-attenders who had an objective goal noted and who returned to the district physician ($n = 33$) attained their goal to a lesser degree, 70 % (chi-square = 5.6, $p < 0.05$).

At the time of referral, the patients were instructed when to return to the district physician. Eighty-eight per cent of all patients studied (Sandby B excluded) returned on time ± 1 month. The remaining 12 % either came later or were called by letter.

Among the non-attenders (Sandby A and B excluded) at the district nurses' ($n = 31$) 81 % consulted the Health Care Centre frequently for chronic diseases other than hypertension and had their blood pressure recorded at these consultations instead.

The structured telephone interview among the 21 patients from DGV (15 %) who discontinued the follow-up at the district nurses' without an acceptable reason noted in their medical records revealed that 16 (76 %) were unaware of being informed about specified intervals for follow-up. They claimed that they were told to go "when convenient". Two blamed the short office hours at the district nurses' (9-11 a.m., 4-4.30 p.m.) for not coming. Two claimed that they had been told by their district physician to discontinue the follow-up although

this was not noted in their medical records. All were aware that they had been informed when to return to the district physician.

Table I. Relative frequency of attendance at the prescribed first visit to district nurses by hypertensives referred by district physicians

	Relative frequency of attendance (%)		
	DGV (n = 140)	Sandby A (n = 49)	Sandby B* (n = 34)
Attendance			
- on time ($\pm$ 1 month)	65	86	71
- not on time (> 1 month)	13	6	0
Non-attendance	22	8	29**

chi sq = 7.50

d.f. = 2, p < 0.05

Table II. Relative frequency of hypertensives in continuing with the follow-up when referred to district nurses

	Relative frequency of follow-up (%)		
	DGV (n = 140)	Sandby A (n = 49)	Sandby B* (n = 34)
Continuous attenders	36	51	56
Discontinued attending			
- with acceptable reasons	27	20	9
- without acceptable reasons	15	20	6
(Non-attenders)	(22)	(8)	(29)

chi sq = 2.35

d.f. = 2, N.S.

*Sandby B not included in the statistical analysis.

** Including 12 % "not time yet".

DISCUSSION

Our results show that fewer than half of all hypertensives referred to the district nurse continued the follow-up throughout the two-year observation period.

Twenty-two per cent of the patients did not attend in three of the areas (DGV). The majority of them (81 %) had other chronic diseases and visited the Health Care Centre repeatedly because of this. They had their blood pressure recorded at these consultations instead of going to the district nurses and should not have been referred.

In one area (Sandby A) there were only 8 % non-attenders. One reason for this difference was probably that the nurses in this area were more active in calling patients who did not attend unrequested. Contributing to these results may be that the author was working one day a week in this area.

The results in Sandby B were as good as in Sandby A, as can be seen from Tables I-II. The observation period in this area, however, was very short.

Lack of information was the major reason for the patients who attended the district nurses' but who discontinued the follow-up without an acceptable reason. This was the case for about 20 % of the patients. All but two of these patients were aware of being referred to the nurses and all were aware of being told when to return to the Health Care Centre.

The patients served as their own controls in this study. All had blood pressure well under control before referral and all had a blood pressure equal to or below the objective of treatment for their age group. In 86 % of those attending, and who had a treatment objective noted on the referral form, this goal was maintained during the study. Among the non-attenders, who had a treatment goal noted on the referral form, a lower percentage, (70 %), had maintained this goal when they returned to the Health Care Centre. Most of these patients had other chronic diseases, some undergoing drug therapy which may have influenced the results.

International comparisons are hazardous because of the appreciable differences in health care systems. In our study we had a high initial attendance rate at the district nurses' (78-92 %) but a relatively low tendency to continue the follow-up during the two-year period (36-51 %). However, 88 % returned to the district physician as scheduled and the remaining 12 % returned either late or after being called. This may be compared with a dropout of 56 % within three months in a study from Atlanta, USA, in 1969 (8) and 50 % within one year in a study reported from Detroit, USA, by Caldwell in 1970 (9).

During the last decade there have been important advances in our understanding of the nature and management of patient compliance in hypertension and other chronic illnesses (10,11). This emphasizes the importance of a record being kept of those hypertensives who are referred for follow-up, so that none is lost because of the referral, as well as the importance of giving information about the intervals for follow-up at every opportunity to both patients and district nurses.

The patients' attitudes were not analysed in this study. It has been shown, however, from our neighbour district (12) that the inhabitants were well aware of the district nurses' daily medical service and were positive to it. More than 90 % regarded measurement of blood pressure as one of the district nurses' tasks.

It has been shown by others (13-15) that most aspects of the management of hypertensives can be delegated to nurses who, providing they accept rational objectives and maintain routine, generally achieve better results than more highly trained medical staff who do not.

In our study, hypertension has been used as an example of a chronic disease which could be followed up by district nurses. Although special instructions were worked out and a lot of information given not all patients attended according to plan, which could in part be explained by the fact that some had concomitant diseases which necessitated visits to the Health Care Centre.

CONCLUSION

Hypertensives above the age of 50 years whose blood pressure is under satisfactory control and who do not require regular visits to the health care centre for other chronic diseases may be referred to district nurses for follow-up without risking loss of control over their blood pressure.

ACKNOWLEDGEMENTS

The author would like to thank professor Bengt Scherstén, Dalby for his valuable support, interest and important advice during the study as well as district physicians and nurses in Dalby Primary Care District for their participation in the study.

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**HIGH RISK OF CEREBRO-CARDIOVASCULAR MORBIDITY IN WELL
TREATED MALE HYPERTENSIVES**

A retrospective study of 40 - 59 year-old hypertensives in a Swedish
primary care district

by

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ABSTRACT

In a retrospective study of 121 hypertensives aged 40-59 years in comparison with 138 controls selected from the population in the same primary care district, male hypertensives had a high odds ratio of cerebro-cardiovascular (CCV) diseases even when their blood pressure had been well treated. The odds ratio (corrected for small numbers) was estimated to 13.7 (2.5-76.7). In females there was a trend towards more CCV diseases among the hypertensives in comparison with their controls.

Although the hypertensives' blood pressure was reduced in accordance with what has been internationally accepted, their values were still at least 10-11 mm Hg higher than those of the controls. A reduction of this magnitude may be accomplished by (further) weight reduction and, probably, by intervention with factors linked to obesity. This may be one way to reduce the excess risk in hypertensives.

Keywords: Hypertension, epidemiology, primary health care, alcohol, smoking, body mass index, drug therapy, gamma-glutamyltransferase

INTRODUCTION

Primary health care ought to be the basis for the long-term management and follow-up of patients with actual and borderline hypertension in Sweden (1).

High blood pressure is a serious risk criterion of cardiovascular morbidity and mortality in the middle-aged especially if other risk factors such as smoking, obesity and excessive alcohol consumption are present (2-3). There is, however, no clearly defined cut-off point for increased risk, since blood pressure is a unimodal and continuous variable (4).

Lowering of high blood pressure is an effective way of reducing morbidity and mortality in both established (5-6) and mild (7-8) hypertension.

In spite of the rather extensive studies published on cardiovascular morbidity in hypertensives (5-8), few have reported on the risk of cerebro-cardiovascular (CCV) morbidity in adequately treated hypertensives, in comparison with non-hypertensive controls. It is therefore interesting to analyse if a small group of carefully studied patients in a defined population in primary health care can be utilized for studies of risk-indicators in a chronic disease like hypertension.

AIMS

The purpose of this study was to investigate whether 40-59-year old hypertensives were adequately treated in a Swedish primary care district, and to analyse the risk of CCV morbidity and its determinants, such as smoking and alcohol habits, obesity etc.

METHODS AND STUDY POPULATION

Study population

All patients born in the period of 1922-41 who visited the Dalby Health Care Centre in 1980 because of actual or borderline hypertension ($n = 156$) were invited to a medical examination in 1981, including a structured interview and various laboratory tests. Of these 152 (97 %) attended the examinations as patients (Fig. 1). They were divided into two groups - hypertensives and borderline hypertensives - according to the diagnosis in their medical records based on the criteria mentioned below.

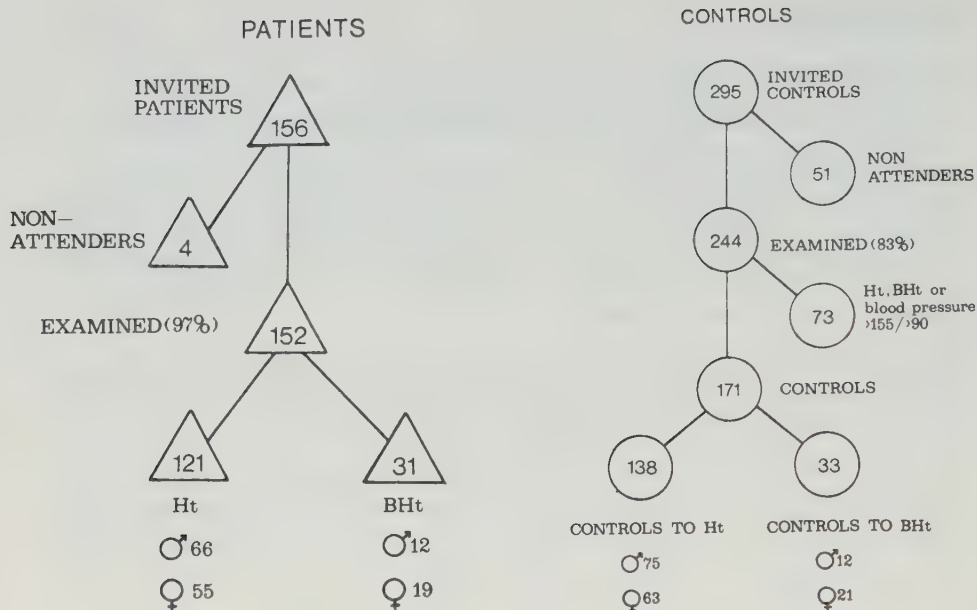


Figure 1. Patients, 40-59 years old, with hypertension (Ht) or borderline hypertension (BHt) invited to medical examinations in 1981, and age- and sex-matched controls invited to the same examinations.

The patients were compared with an age- and sex-matched control group chosen from the same primary care district with the aid of the official population register. All inhabitants in the primary care district are listed in this register in chronological order. For each patient who attended the medical examinations, persons of the same sex located before and after the patient in the population register were selected as controls. In this way 295 persons born the same year and month as the patients - and mostly also on the same day - comprised the control group, of whom 244 (83 %) attended (Fig. 1). All comparisons were made between the group of patients and the group of controls.

Controls who had a diagnosis of hypertension or borderline hypertension as well as those who had a systolic blood pressure exceeding 155 mm Hg or a diastolic blood pressure exceeding 90 mm Hg, at any of two examinations - on separate days - were not accepted in the analyses. Altogether 73 control persons were excluded (Fig. 1, 2).

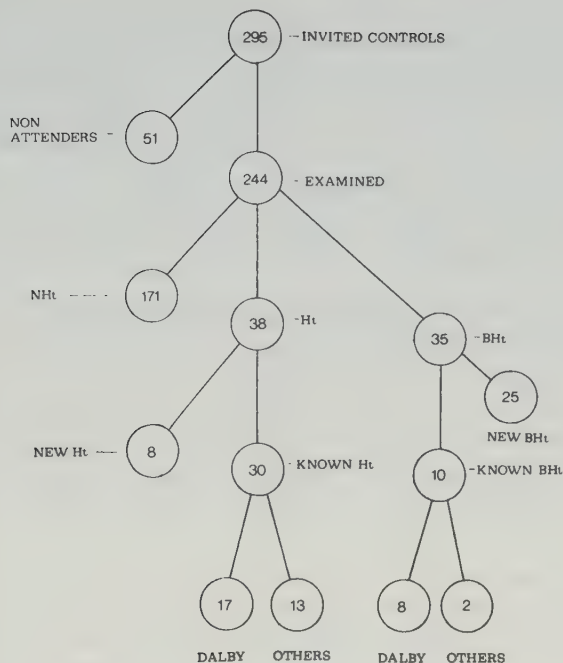


Figure 2. Number of hypertensives (Ht) and borderline hypertensives (BHt), 40-59 years old, in the control material consulting the Dalby Health Care Centre (DALBY) and other physicians (OTHERS) for their hypertension. NHt = Non-hypertensives.

Organization

Patients and controls were first interviewed by a single specially trained nurse concerning their medication and their smoking as well as alcohol habits. Blood pressure was measured in the right arm after 5-10 minutes of rest in a recumbent position and after 2 minutes' standing. Diastolic blood pressure values were phase V.

Blood samples were drawn at random with standard Vacutainer technique and total bilirubin (S-Bil, $\mu\text{mol/l}$), alkaline phosphatase (S-ALP, $\mu\text{Kat/l}$), gamma-glutamyltransferase (S-GT, $\mu\text{Kat/l}$), alanine aminotransferase (S-ALAT, $\mu\text{Kat/l}$) and aspartate aminotransferase (S-ASAT, $\mu\text{Kat/l}$) were analysed at the Department of Clinical Chemistry, University Hospital, Lund. Body weight (w,kg) and height (h,m) were measured and the body mass index (w/h^2) was calculated.

All patients and controls were then seen by a physician (LL) who made a conventional examination. Anamnestic data, including past history of diseases, were recorded for all attenders at a structured interview and were checked against the medical records at the Health Care Centre as well as those at Lund University Hospital. Medical records of all non-attenders were sought and studied at the Health Care Centre, at the University Hospital and at private practitioners when indicated.

Criteria for diagnoses of hypertension and borderline hypertension

At the Health Care Centre in Dalby the blood pressure limits used in the daily routine for asymptomatic patients aged 40-59 years were (mean of at least three measurements): for hypertension $> 170 / > 105$ mm Hg, and for borderline hypertension 160-170/95-105 mm Hg. If the patient had diabetes the limits were 5-10 mm Hg lower.

Objective of treatment

The aim of treatment in the age group 40-59 years was to establish a level of $\leq 160 / \leq 95$ mm Hg. In diabetics, the aim was generally 5-10 mm Hg lower.

Non-attending patients and controls

Of 156 patients invited to the medical examinations 4 failed to attend. They had no history of CCV disease. Information was obtained about 39 (76 %) of the 51 non-attending controls from records at the hospital as well as at the Health Care Centre. Two male patients had hypertension. The prevalence of CCV diseases did not differ when attending controls were compared with non-attenders (chi-square 0.86 or below).

Representativity of the hypertensive cases

There were 30 previously diagnosed hypertensives in the control material (Fig. 2). Seventeen of them were seen at the Health Care Centre and 13 consulted other physicians. When these 17 patients were compared with all other hypertensive patients in the study as well as with the 13 hypertensives who consulted other physicians, no significant differences were found ($|t| < 0.9$, chi-square < 1.0 , N.S.) regarding age, sex, body mass index, blood pressure, pulse, laboratory tests, CCV diseases, smoking and alcohol habits or in the percentage who attained their treatment objective. Although only about two-thirds of the hypertensives in this age group consulted the Health Care Centre, these

comparisons indicate that the patients were representative of all hypertensives in the primary care district.

Data processing and statistical methods

All data were stored, structured and analysed by using the SPSS Program System on a large Univac Computer 1100/80. Student's t -test was used to test the hypothesis of no difference in mean values between two groups and to test the hypothesis of no correlation between variables. The normal deviate test was used to test the hypothesis of no difference between proportions where the normal distribution was used as an approximation of the binomial distribution.

In order to test the difference between frequencies in two or more groups, the Chi-square test was used. Yates' correction for continuity was used where any of the expected frequencies was less than five, for one degree of freedom.

Partial correlation analysis was used to describe the linear relationship between two variables when the influence of other variables had been eliminated (9). These results were expressed as partial correlation coefficients. The dependent variable was blood pressure group and the independent variables were body mass index, age, alcohol habits, smoking habits and S-GT chosen as an indicator of alcohol consumption (10). Since blood pressure group was measured on an ordinal scale, the relationship between S-GT and blood pressure group was checked with an analysis of variance. In a multiple regression analysis the correlation between the dependent variable and all independent variables was compared.

Patients and controls treated with enzyme inductors such as anticonvulsive drugs, psychopharmaca and contraceptives were excluded from the correlation analysis together with diabetics because of possible interference with the S-GT analyses (10).

Statistical significance was evaluated at the levels $p < 0.05$, < 0.01 and < 0.001 . A difference was considered statistically significant when the p -value was < 0.05 .

The relative odds of a CCV disease was estimated and corrected for small numbers as shown in Fig. 3. The confidence limits were estimated as recommended by Lilienfeld (11). These estimates proved relevant, since both patients and controls were selected in a known way and from the same population as described in Methods.

	Hypertensives	Controls
with characteristic	a	b
without characteristic	c	d

$$\psi = \frac{\frac{a}{b}}{\frac{c}{d}} = \frac{a \cdot d}{b \cdot c}$$

$$\psi_c = \frac{(a + 0.5) \cdot (d + 0.5)}{(b + 0.5) \cdot (c + 0.5)}$$

Figure 3. Estimation of relative odds (ψ) and corrected relative odds (ψ_c) of cerebro-cardiovascular diseases (CCV) in hypertensives and controls; **a, b, c and d** indicate numbers.

RESULTS

Coronary heart disease (myocardial infarction + angina pectoris) was more common among male hypertensives aged 40-59 years than among their controls (Table I, $p < 0.001$). This was not the case in females. When all CCV diseases (myocardial infarction, angina pectoris, symptomatic heart diseases, stroke and intermittent claudication) were considered together, these were more common in male hypertensives than in their controls (Table I, $p < 0.001$). In women there was a trend toward more CCV diseases among hypertensives than among their controls (chi-square raw 4.76, $p < 0.05$; chi-square, corrected 2.66, N.S.).

The corrected odds ratio of CCV diseases in male hypertensives was estimated to 13.7 (95 %, confidence interval 2.5-76.7).

Table I. Comparison of the frequencies of cerebro-cardiovascular diseases (CCV), stroke, coronary heart disease (angina pectoris and myocardial infarction), claudicatio intermittens and diabetes in male and female hypertensives, 40-59 years old, with their age- and sex-matched controls; p indicates the level of significance (Chi sq test).

Disease	Frequencies (%)		
	Patients	Controls	p
<u>Male</u>	(n=66)	(N=75)	
CCV disease	21	1	< 0.001
- stroke	2	0	N.S.
- coronary heart disease	20	1	< 0.001
- claudicatio	2	0	N.S.
Diabetes	8	5	N.S.
<u>Female</u>	(n= 55)	(n=63)	
CCV disease	8	0	N.S. ¹
- stroke	4	0	N.S.
- coronary heart disease	2	0	N.S.
- claudicatio	2	0	N.S.
Diabetes	5	2	N.S.

¹ chi sq (corrected) 2.7, N.S. chi sq (raw) 4.8 p < 0.05

Two-thirds of the hypertensives with CCV complications had their hypertension diagnosed before, and one-third at the time of the complication(s). The latter diagnoses were confirmed in the medical records at the University Hospital in Lund (Departments of Cardiology, Internal Medicine, Neurology and Surgery).

There were no differences (chi-square = 0, N.S.) in the percentage of patients who attained their treatment objectives when hypertensives with vs. without CCV complications were compared. The smoking habits in these groups did not differ (chi-square = 2.21, d.f. = 2, N.S.).

Blood pressure recordings before drug treatment was instituted were found in the medical records in 60 of 66 male hypertensives and in 46 of 55 females. The last value noted was used in the comparison in this study. Hypertension was diagnosed (mean $\pm$ SD) 6.5 $\pm$ 5.4 years (males) and 7.3 $\pm$ 5.9 years (females) before this study.

Table II. Blood pressure (dx), mean $\pm$ SE (mm Hg) before and during treatment in male and female hypertensives, 40-59 years old in comparison with their age- and sex-matched controls; p indicates the level of significance (two tailed t-test).

	Before treatment (B)	During treatment (D)	Controls (C)	p < 0.001
<u>Male</u>	(n=60)	(n=66)	(n=75)	
Systolic	183 $\pm$ 2.1	149 $\pm$ 2.0	133 $\pm$ 1.4	B vs. D D vs. C
Diastolic	114 $\pm$ 1.2	91 $\pm$ 1.0	80 $\pm$ 0.9	B vs. D D vs. C
<u>Female</u>	(n=46)	(n=55)	(n=63)	
Systolic	187 $\pm$ 2.8	154 $\pm$ 2.6	134 $\pm$ 1.6	B vs. D D vs. C
Diastolic	110 $\pm$ 1.3	91 $\pm$ 1.1	80 $\pm$ 0.8	B vs. D D vs. C

Both systolic and diastolic blood pressure were considerably lower during treatment than before it ($p < 0.001$), the mean reduction being 34/23 mm Hg in males and 33/19 mm Hg in females (Table II). Ninety-three per cent of all patients were treated with antihypertensive drugs; 75 % received betablocking agents, 42 % diuretics and 12 % hydralazine.

In comparison with their controls hypertensives had higher ($p < 0.001$) blood pressure values during treatment, in males 16/11 mm Hg, and in females 20/11 mm Hg (Table II).

At the examination in 1981 the agreed treatment objective for hypertensives aged 40-59 years - blood pressure $\leq 160/\leq 95$ mm Hg or below - was attained by 73 % of both the male and the female patients.

The smoking habits differed between patients and controls in males - but not in females. There were more ex-smokers among male patients (47 % vis-à-vis 31 %; $z = 1.99$, $p < 0.05$) and a trend towards fewer smokers (21 % vis-à-vis 36 %, $z = 1.93$, $p = 0.054$). The number of non-smokers did not differ between the groups (32 and 33 % respectively, N.S.).

The admitted alcohol habits did not differ between hypertensives and controls (males and females) (chi-square 1.9-4.1, d.f. = 2, N.S.). Nor did the calculated alcohol consumption the week before the examinations (Table III). S-GT was higher in male and female hypertensives than in their controls (Table III, $p < 0.01$ and $p < 0.001$, respectively). S-ALAT and S-ASAT levels were also higher in hypertensives than in their controls ($p < 0.001$), S-GT correlated ($p < 0.001$) with S-ASAT for both males and females ($r = 0.78$ and 0.33) and also with S-ALAT ($r = 0.78$ and 0.46).

Hypertensives of both sexes had a higher body mass index than their controls ($p < 0.001$, Table III).

Table III. Comparison (mean $\pm$ SE) of age (years), body mass index (w/h^2 , kg/m) alcohol consumption (grams 100 % alcohol), S-GT (μ Kat/l), S-ASAT (μ Kat/l, S-ALAT (μ Kat/l), S-Bil (μ mol/l) and S-ALP (μ Kat/l) in male and female hypertensives, 40-59 years old, with their age- and sex-matched controls; p indicates the level of significance (two tailed t-test).

Variables	Males			Females		
	Patients (n=66)	Controls (n=75)	p	Patients (n=55)	Controls (n=63)	p
Age	51.6 $\pm$ 0.6	51.0 $\pm$ 0.5		52.2 $\pm$ 0.7	50.9 $\pm$ 0.7	
w/h^2	28.4 $\pm$ 0.4	25.0 $\pm$ 0.3	< 0.001	28.1 $\pm$ 0.7	25.2 $\pm$ 0.5	< 0.001
Alcohol	47.8 $\pm$ 9.2	41.4 $\pm$ 7.8	N.S.	8.0 $\pm$ 1.9	11.8 $\pm$ 3.1	N.S.
S-GT	0.78 $\pm$ 0.07	0.53 $\pm$ 0.06	< 0.01	0.54 $\pm$ 0.07	0.28 $\pm$ 0.02	< 0.001
S-ALAT	0.53 $\pm$ 0.03	0.39 $\pm$ 0.02	< 0.001	0.41 $\pm$ 0.02	0.30 $\pm$ 0.02	< 0.001
S-ASAT	0.44 $\pm$ 0.02	0.37 $\pm$ 0.01	= 0.001	0.39 $\pm$ 0.01	0.33 $\pm$ 0.01	= 0.001
S-Bil	13.0 $\pm$ 0.6	12.3 $\pm$ 0.7	N.S.	12.0 $\pm$ 1.4	9.7 $\pm$ 0.5	N.S.
S-ALP	3.2 $\pm$ 0.1	3.0 $\pm$ 0.1	N.S.	3.1 $\pm$ 0.1	2.8 $\pm$ 0.1	N.S.

When the blood pressure group was correlated to a linear function of age, smoking and alcohol habits, S-GT and body mass index, the multiple correlation coefficients in males and females were 0.47 ($p < 0.01$) and 0.41 ($p < 0.001$), respectively. The partial correlation coefficients are listed in Table IV. Body mass index showed the closest correlation to blood pressure group in males, and S-GT in females.

Table IV. Partial correlation coefficients between blood pressure group¹⁾ and body mass index (w/h^2 , kg/m), alcohol habits (1-6)²⁾, smoking habits (1-4)³⁾, S-GT ($\mu\text{Kat/l}$), and age (years) respectively in 366 males and females, 40-59 years old; p indicates the level of significance (two tailed t-test).

	Partial correlation coefficients			
	Males (n=183)		Females (n=153)	
	r	p	r	p
w/h^2	0.39	< 0.001	0.17	< 0.05
Alcohol habits	0.05	N.S.	-0.20	< 0.01
Smoking habits	-0.13	= 0.05	0.03	N.S.
S-GT	0.07	N.S.	0.20	< 0.01
Age	0.14	< 0.05	0.03	N.S.

1) non-hypertensive = 1, borderline = 2, hypertensive = 3

2) alcohol habits (strong beer, wine and liquor): never = 1, < once/month = 2, 1-3 times/month = 3, once/week = 4, several times/week = 5, every day = 6

3) non-smoker = 1, ex-smoker = 2, light smoker (≤ 14 cig/day) = 3, heavy smoker (≥ 15 cig/day) = 4

DISCUSSION

This study has shown that a limited number of patients in a defined population in primary health care can be utilized in epidemiological studies regarding risk and may therefore justify this model for studies in primary health care.

Our results show that male hypertensives have a high risk of CCV diseases even when their blood pressure had been adequately reduced. This was still, however, about 16/11 mm Hg higher than in the controls.

The odds ratio (corrected for small numbers) in this study was estimated to 13.7 (2.5-76.7) in males. In females there was a trend toward more CCV diseases which did not reach significance when hypertensives were compared with their controls. To avoid a type II fallacy it should be underlined that this may be explained by the limited numbers and does not indicate that hypertension is unassociated with CCV disease in women. However, earlier epidemiological studies have shown that the prognosis of hypertension in females is better than in males (12).

One explanation for the excess risk in male hypertensives may be that their blood pressure has not been sufficiently reduced. The HDFFP-study Group has reported (7) a beneficial effect of stepped care treatment in males without evidence of end-organ damage and with diastolic pressures of 90 to 104 mm Hg. The Australian Therapeutic Trial (8) has shown an effect of treatment on cardiovascular morbidity and mortality in male hypertensives with diastolic blood pressures of 100 mm Hg and above. No effects were demonstrated in white women in either study.

Our results are in accordance with data from the 20-year follow-up in the Framingham study (13), where hypertensives (blood pressure $\geq 160/\geq 95$ mm Hg) had experienced cardiovascular diseases three times more often than normotensives (blood pressure $< 140/< 90$ mm Hg). Our male hypertensives had a blood pressure during treatment of about 149/91 mm Hg in comparison with 133/80 mm Hg in the controls. This may be compared with The 1979 Build and Blood Pressure Study (14), comparing four million non-hypertensive and 26,000 hypertensive policy holders in U.S.A. The **mortality** ratio in treated hypertensives with systolic blood pressure in the group 148-157 mm Hg was 170, in comparison with 111 in the group 128-137 mm Hg. The latter figure was the same as in non-hypertensives in the corresponding group.

A further blood pressure reduction in our patients may be achieved with an intensified drug therapy. The patients' blood pressure during treatment was 20-16/11 mm Hg higher than their age- and sex-matched controls. Intensified drug therapy, however, can lead to an increase in adverse effects (15) which may seriously disturb the patients' quality of life and interfere with their compliance.

The high odds ratio of the patients in this study may also be viewed against the background circumstance that all hypertensives in the Health Care Centre have been recommended a low-calorie and low-sodium diet, as well as to stop smoking and reduce their alcohol consumption (when indicated). The Oslo study (16) of a high risk group of males has shown an effect on cardiovascular morbidity and mortality after a change in diet with a reduction of saturated fat and calories as well as a reduction of smoking. In our study the degree of obesity was higher among the patients than in their controls even though instructions regarding diet had been given (Table III).

The hypertensives had higher S-GT, S-ASAT and S-ALAT values than did their controls (Table III) but there were no differences in S-Bil and S-ALP between the groups. These findings are in agreement with what has been published in studies on middle-aged males in Malmö, the third largest city in Sweden (17-18). There were, however, 38 % abnormal S-GT values ($> 1.1 \mu\text{Kat/l}$) among the hypertensives in the Malmö studies in comparison with 20 % in the present study. These results may be explained by a difference in drinking habits in males in a large city such as Malmö and a rural area like Dalby.

There was no partial correlation between blood pressure group and alcohol habits in males in our studies; whereas there was a negative partial correlation in females (Table IV). As regards blood pressure group vs. smoking habits, there was a negative partial correlation in males, but no correlation in females (Table IV). As there were no differences in alcohol habits in either sex, and as there tended to be fewer smokers and there were more ex-smokers among male hypertensives, these findings suggest that further attempts to influence alcohol and smoking habits in the patients as a group would be of limited value. On the other hand, since there is a partial correlation between blood pressure group and body mass index in both sexes, it would seem more appropriate to reduce the degree of fatness or affect factors which may be linked to this such as sodium/potassium intake, circulating insulin levels etc. (19-20).

Although the hypertensives' blood pressure was reduced in accordance with what has been internationally accepted, their values were still at least 10-11 mm Hg higher than those of the controls. A reduction of this magnitude may be accomplished by (further) weight reduction and, probably, by intervention with factors linked to obesity. This may be one way to reduce the excess risk in hypertensives. However, this will necessitate documentation through further studies.

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Hypertension in Elderly People in a Swedish Primary Care District

by

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ABSTRACT. In a retrospective study, 124 hypertensives aged 60-69 years, and taken care of by primary health care, were compared with 124 age and sex matched controls with regard to blood pressure, body mass index, smoking and alcohol habits as well as cardiovascular diseases. Blood pressure, mean $\pm$ SEM (mm Hg) was reduced by 37/24 in males and 40/24 in females. Drug treatment was given to 93 per cent of the patients. Our goal of treatment - blood pressure 180/100 or below - was obtained in 75 per cent of the patients. Cardiovascular diseases were more common in male hypertensives than in their controls. The relative odds of stroke in male hypertensives treated within the primary health care organisation was estimated to 7.7 (1.3-45.3) and of cardiovascular diseases to 4.3 (1.7-10.1).

In a ten year prospective cohort study of all pensioners in the primary care district, born in 1902 and 1903, a subcohort of pensioners with hypertension and under medical treatment when they were 70 years old ($n = 39$) was compared with the subcohort of pensioners without hypertension at this age ($n = 105$). This study comprised 342 person-years in the former subcohort and 889 person-years in the latter. No significant differences in mortality nor in cardiovascular morbidity were found between the subcohorts.

The results of the two studies showed higher risks for male hypertensives aged 60-69 years who are taken care of by primary health care compared with those aged 70-80 years in spite of the latter group being older, having higher systolic blood pressure at the examinations and less degree of anti-hypertensive drug treatment. This shows that hypertension as a risk indicator for cardiovascular diseases may differ between age groups above 60 years.

KEY WORDS: Hypertension. Epidemiology. Elderly. Primary health care. Drug treatment. Alcohol. Weight. Smoking. Morbidity. Mortality.

INTRODUCTION

Blood pressure in the population is a unimodal and continuously rising variable and the risks of morbidity and mortality increase with rising pressure, there being no clearly defined cut off point for increased risk (1). Several studies (2-4) have shown that hypertension is an important risk factor for cardiovascular diseases, notably coronary-artery disease, heart failure and stroke below the age of 70 years.

Regarding ages above 70 years few studies have reported on morbidity and mortality of patients with hypertension. In the Framingham studies (2), the hypertensive patients in the subgroup aged 65-74 years had an annual incidence of cardiovascular disease three times greater than the normotensive persons. Whether pharmacological lowering of the blood pressure in the age group above 70 years can reduce morbidity and prolong life is still a controversy...

The demographic pattern in Sweden, like in most countries, is changing, and elderly people aged 70 to 80 years are increasing in numbers as well as in percentage of the patient population (5). In Sweden primary health care will be responsible for the health and medical care of all inhabitants in the primary care district. One of the main objectives of primary health care must be to keep the old from becoming ill and to maintain their independence and quality of life. Especially stroke and symptomatic heart diseases must be prevented whenever possible.

This paper comprises two studies: A retrospective

study of hypertensive patients aged 60 to 69 years in comparison with controls, and a ten year prospective cohort study of pensioners aged 70 to 80 years, dichotomized into those with a diagnosis of hypertension at the age of 70 years and those without.

Our aim is to describe hypertensive patients aged 60 to 69 years, who are taken care of by primary health care and to compare them with a perfectly age and sex matched control group with regard to blood pressure, body mass index, smoking and alcohol habits as well as cardiovascular diseases and diabetes. We also aim to describe the risk of mortality and morbidity in pensioners aged 70 to 80 years with hypertension under medical treatment, when they were 70 years old, compared with pensioners without hypertension at that age.

METHODS AND SELECTION OF PATIENTS AND CONTROLS

Criteria for diagnoses of hypertension and borderline hypertension

At the Health Care Centre in Dalby the blood pressure limits used in the daily routine for unsymptomatic patients aged 60 or more were (mean of at least three measurements) for hypertension $>180/>110$ mm Hg and for borderline hypertension $170-180/105-110$ mm Hg. If the patient had signs of end organ damage or diabetes the limits were 5 to 10 mm Hg lower.

Retrospective study of hypertensive patients and controls born in 1912-1921

All patients born in 1912-1921 who visited the Dalby Health Care Centre in 1980 for hypertension or borderline hypertension ($n = 157$) were invited to a medical examination in 1981 including a structured interview and laboratory tests. Of these 148 (94%) attended the examinations (Fig. 1). They were divided into two groups - hypertensives and borderline hypertensives - according to the diagnoses in their medical records based on the criterias mentioned above.

The patients were compared with an age and sex matched control group chosen from the same primary care district with the help of the official population register. All inhabitants in the primary care district are listed in this register in chronological order. For each patient who attended the medical examinations the persons of the same sex located before and after

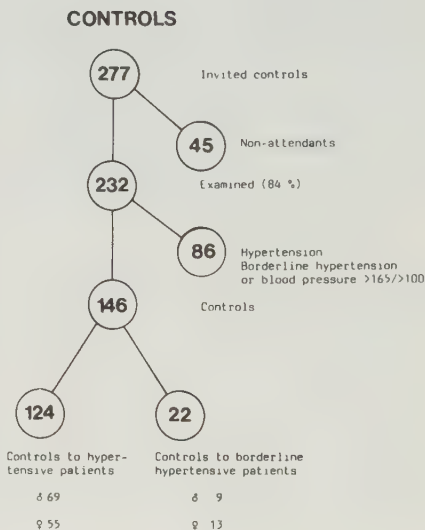
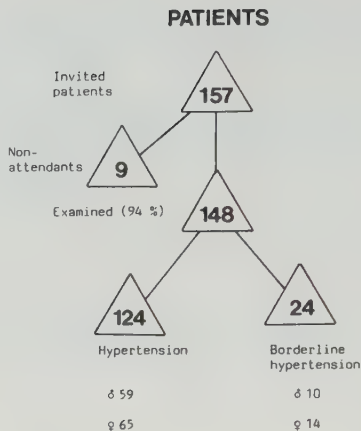


Fig. 1. Patients born in 1912-1921 with hypertension or borderline hypertension invited to a medical examination and age and sex matched controls invited to the same examination.

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the patient in the population register of the primary care district were chosen as controls. Thus, the control material was selected from the population by the paired sampling technique with two controls for each patient. In this way 296 persons born in the same year and month as the patients and mostly also on the same day comprised the control group. In 17 cases, however, one control was shared by two patients who had civic registration numbers near each other and two controls were not invited for technical reasons, why the invited control group amounted to 277 persons of whom 84% attended (Fig. 1). All but ten controls (two males and eight females) had medical records at the Health Care Centre before the examinations.

The patients and controls were first interviewed carefully by one specially trained nurse about, among other things, their smoking and alcohol habits. The smoking habits were graded in smokers, ex-smokers and non-smokers. The alcohol habits were classified in three groups according to the use of strong beer, wine, and liquor; less than once per month, once per month to once per week, and several times per week. Furthermore, the admitted alcohol-consumption the week before the medical examination was calculated in grams of pure alcohol from all types of alcoholic beverages.

Throughout the study the blood pressure was measured with the same mercury manometer, in both arms after five to ten minutes of rest in a recumbent position, and in the right arm after two minutes in a standing posture. The cuff breadth was adjusted according to the arm circumference (6). Diastolic blood pressure values were phase V. The heart rate was registered after five to ten minutes of rest lying down.

Blood samples were drawn with standard vacutainer technique. The body weight (w) and height (h) were measured, and the body mass index (w/h^2) was calculated.

If B-glucose (at random) was 7.0 mmol/l or more, two fasting B-glucose tests were made on separate days. If both were 7.0 mmol/l or above diabetes mellitus was diagnosed, and the patient was referred to a further follow-up at the Health Care Centre. A fasting B-glucose below 5.5 mmol/l was considered to be normal. If fasting B-glucose was between 5.5 and 7.0 mmol/l an oral glucose test was made.

All patients and controls were seen by the physician who made a conventional clinical examination. Anamnestic data were obtained by interview and review of the medical records at the Health Care Centre

and at the Lund University Hospital. Current treatment with drugs was registered.

If the systolic pressure exceeded 165 mm Hg and/or the diastolic pressure exceeded 100 mm Hg at any of two examinations, a control was not accepted in the analyses.

Analysis of non-attending patients and controls, and of "excluded controls"

Of 157 patients invited to the medical examinations nine (two males and seven females) did not attend. It was found that eight out of nine had drug treatment for their hypertension. One female had a history of stroke and heart disease and another had diabetes. The blood pressure was below 180/100 in all but one non-attending patient.

Information was obtained about 37 (82%) of the 45 non-attending controls. One (0.4% of 277) had a diagnosis of hypertension, and three (one % of 277) of borderline hypertension. The occurrence of stroke, symptomatic heart disease, myocardial infarction, and diabetes did not differ, when attending controls were compared with non-attending (chi square 1.27 or below).

In the control-material, chosen from the same population as the patients, 51 persons (18.4% of 277) had hypertension. Forty of them had been examined as "hypertensive patients" in the study, seven consulted other physicians for hypertension and four were newly diagnosed. Thirty-five (12.6% of 277) had borderline hypertension. Eleven of them had been examined as "patients" and 24 were newly diagnosed. Altogether 86 (31% of 277) were therefore excluded as controls in the analyses. Since the proportion of the population in each year group in the control material varied to a low degree, the prevalence of hypertension could be estimated to 18.8 (0.4 + 18.4) % in the year 1981 in this area of Sweden. The corresponding figures for borderline hypertension were 13.6 (1.0 + 12.6) %.

Borderline hypertension is not further considered in the study.

Analysis of the representativity of the hypertensive patients in the population

The design of the study allows an estimation of the percentage of hypertensives taken care of outside the Health Care Centre. As mentioned above, seven out

of 47 known hypertensives in the control material consulted other physicians, that is about 15 %. To investigate the representativity of our hypertensives the county council register of patients with stroke in hospital care – with and without hypertension – was analysed for the years 1977–1981. All patients but one with stroke and hypertension were in our study. No patient with stroke without hypertension was a patient in our study. Against this background our patients were considered representative of the hypertensives in the population.

Prospective cohort study of pensioners born in 1902 and 1903

In 1969 and 1970, respectively, an extensive study was started of all pensioners born in 1902 and 1903 and living in the Dalby district (7, 8). The patient material consisted of 156 pensioners or 82 per cent of the target population (Fig. 2). They have been subjected to

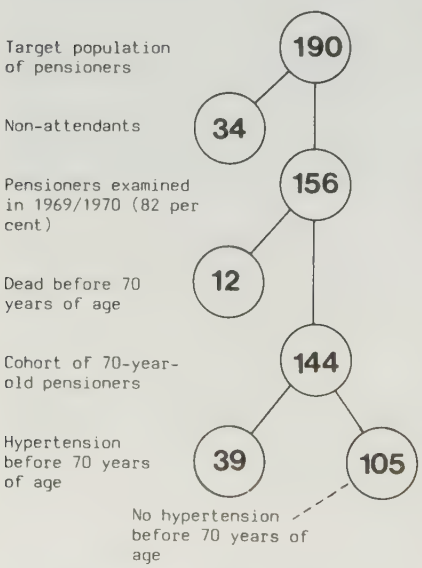


Fig. 2. Target population of pensioners born in 1902 and 1903, invited to medical examinations in 1969/1970, and establishment of a cohort of 70-year-old pensioners, dichotomized into those with and without hypertension at the age of 70 years, aimed for a prospective study.

follow-up examinations every second year since then. Of these 156 pensioners 144 reached the age of 70 years in 1972/1973. This group established our cohort of pensioners used for a ten year prospective study from 1972/1973.

The cohort was dichotomized into those who had established hypertension at the age of 70 years (n = 39) and those without (n = 105). These groups were used for comparison of the survival rate and the occurrence of myocardial infarction, stroke, symptomatic heart diseases and diabetes.

The medical examinations performed in the pensioner group have been described elsewhere (7, 8). After at least ten minutes of rest blood pressure was measured in a recumbent position with a mercury manometer and a 12 x 26 cm cuff. Until 1976 it was measured in the right or the left arm, and the cuff breadth was not adjusted according to the arm circumference. From 1978 the blood pressure was measured in the right arm after 5 – 10 minutes of rest with the cuff breadth adjusted to the arm circumference (6).

Information was obtained from the Health Care Centre, hospitals, private practitioners, autopsy protocols, and death certificates.

The 34 pensioners not attending the first examination in 1969/1970 were followed up by their medical records at the Health Care Centre as well as at the Lund University Hospital. The autopsy protocols and death certificates were also studied.

Data processing and statistical methods

All data were stored, structured and analysed by using the SPSS Program System on a large Univac Computer (1100/80). Student's t-test was used to test the hypothesis of no difference in mean values between two groups (e.g. in Tables I and II). Chi square-test was used to test the hypothesis of no difference between frequencies (e.g. Table III). Yates' correction for continuity was used where any of the expected frequencies was less than five for one degree of freedom. The McNemar chi square-test was used in matched-pair analyses. Normal deviate test was used to test the hypothesis of no difference in mean values between the two groups in the comparison of calculated alcohol consumption the week before the medical examination.

The statistical significance was evaluated by two-tailed tests at the levels $p < 0.05$, $p < 0.01$, $p < 0.001$. A difference was considered statistically significant if

the *p* value was < 0.05 .

The odds ratios of cardiovascular diseases were estimated in the retrospective study (9). These estimates were relevant since both the patients and controls were representative of their populations. The mortality rate and ten year cumulative incidence rates of stroke, symptomatic heart diseases, myocardial infarction and diabetes were calculated in the cohort study as described by Mac Mahon (9).

RESULTS

Retrospective study

Recordings of raised blood pressure before drug treatment were found in 50 out of 59 male patients and in 43 out of 65 female patients. The last values before treatment was started were used.

As can be seen in table I both systolic and diastolic blood pressures were considerably lower during treatment than before ($p < 0.001$), the mean reduction being 37/24 mm Hg in males and 40/24 mm Hg in females. The corresponding values were 36/24 and 37/22 mm Hg respectively, if only patients with a before-treatment-value were included in the comparison. The level of significance was the same ($p < 0.001$).

In comparison with their controls (Table I) the blood pressures in hypertensive males were 19/11 mm Hg and in females 21/9 mm Hg higher ($p < 0.001$).

At the examination in 1981 the agreed goal of treatment of hypertension in patients aged 60 – 69 years i.e. blood pressure 180/100 mm Hg or below, was reached by 76 % of the male and 75 % of the female patients.

Systolic blood pressure (mean mm Hg $\pm$ SEM) in standing posture was 148 ± 2.5 in male patients, 129 ± 1.8 in male controls, 151 ± 2.8 in female patients and 136 ± 2.3 in female controls. In comparison with recumbent position systolic blood pressure was 12 mm Hg lower in male patients ($p < 0.001$) as well as in controls ($p < 0.001$). In female patients the difference was 14 mm Hg ($p < 0.001$) and in female controls 8 mm Hg ($p < 0.01$). This difference between female patients and controls was statistically significant ($p < 0.05$). There were no differences in diastolic blood pressure in any sex.

Heart rate (mean $\pm$ SEM) was lower ($p < 0.05$) in the male patients during treatment (67 ± 1.2) than in their controls (70 ± 0.9). This was not the case in female patients (71 ± 2.0) compared with their controls (74 ± 1.0).

Of all the hypertensive patients ($n = 124$) 56% were treated with one antihypertensive drug, 35% with two, and two % with three or more antihypertensive drugs. Seven % were not treated with any antihypertensive drug. The number of drugs in male and female patients did not differ.

Hypertensive patients of both sexes had higher body mass index than their controls ($p < 0.001$ and p

Table I. Blood pressure, mean $\pm$ SEM (mmHg) before and during treatment of hypertension in male and female patients born in 1912–21, visiting Dalby Health Care Centre in 1980, in comparison with their age and sex matched controls. P indicates the level of significance (two tailed t-test).

Sex	Numbers and blood pressure	Before treatment (B)	During treatment (D)	Controls (C)	<i>p</i> < 0.001
Male	(n)	(50)	(59)	(69)	
	systolic	197 ± 2.7	160 ± 2.3	141 ± 1.4	B vs D, D vs C
	diastolic	116 ± 1.7	92 ± 1.1	81 ± 1.0	B vs D, D vs C
Female	(n)	(43)	(65)	(55)	
	systolic	205 ± 3.9	165 ± 2.2	144 ± 1.6	B vs D, D vs C
	diastolic	115 ± 1.8	91 ± 1.2	82 ± 0.9	B vs D, D vs C

< 0.01, Table II).

The smoking habits of the patients differed from those of their controls in women but not in men. Thus, three % of the female patients were smokers compared with 18 % of their controls ($p < 0.05$). The percentage of ex-smokers did not differ between patients and controls.

The admitted alcohol habits of the patients and controls did not differ significantly (chi square 2.29 – 2.56). The calculated alcohol consumption, mean $\pm$ SEM (grams 100 per cent alcohol) the week before the examination was 41.7 ± 9.7 and 27.9 ± 5.2 (NS) in male patients and their controls and 6.7 ± 2.1 and 4.9 ± 2.0 (NS) in female patients and their controls. The serum gammaglutamyltransferase (S-GT), mean $\pm$ SEM ($\mu\text{Kat/l}$) was 0.60 ± 0.05 and 0.55 ± 0.06 (NS) in male patients and their controls and 0.48 ± 0.05 and 0.41 ± 0.04 (NS) in female patients and their controls.

Stroke was more frequent in male patients ($p < 0.05$) than in their controls (Table III). This was not the case in women. There were no significant differences in the frequencies of myocardial infarction, symptomatic heart diseases or diabetes in neither sex, although there was a trend of more frequent symptomatic heart diseases in female patients in comparison with their controls (chi square raw 3.92 $p < 0.05$, chi square corrected 2.60 NS).

When the patients were compared with their controls in a matched-pair analysis, stroke and diabetes were more frequent in male patients (chi square 7.0, $p < 0.01$ and chi square 4.50, $p < 0.05$). There were no differences in women.

Two unknown cases of diabetes (one male and one female) were diagnosed among the hypertensive patients. No cases were found among the controls.

The odds ratio (corrected) of stroke in male patients aged 60 – 69 years was estimated to 7.7 (95%

Table II. Age, mean $\pm$ SEM (years) and body mass index (w/h^2), mean $\pm$ SEM (kg/m) in 124 hypertensive patients born in 1912–21 visiting Dalby Health Care Centre in 1980 compared with their age and sex matched controls. P indicates the level of significance (two-tailed t-test).

Variables	Male		p	Female		p
	Patients (n=59)	Controls (n=69)		Patients (n=65)	Controls (n=55)	
Age	64.3 ± 0.4	64.7 ± 0.3		64.9 ± 0.4	64.6 ± 0.4	
w/h^2	28.0 ± 0.5	25.4 ± 0.4	< 0.001	29.5 ± 0.7	26.7 ± 0.7	< 0.01

Table III. Frequencies of stroke, symptomatic heart disease, myocardial infarction and diabetes in 58¹ male and 64¹ female hypertensive patients born in 1912–21 visiting Dalby Health Care Centre in 1980, in comparison with their age and sex matched controls. P indicates the level of significance (chi square test).

Sex	Disease	Patients	Controls	P
Male	(n)	(58)	(69)	
	Stroke	14%	1%	$< 0.05^2$
	Symptomatic heart disease	12%	6%	NS
	Myocardial infarction	17%	7%	NS
	Diabetes	16%	6%	NS
Female	(n)	(64)	(55)	
	Stroke	2%	2%	NS
	Symptomatic heart disease	11%	2%	NS ³
	Myocardial infarction	3%	2%	NS
	Diabetes	11%	4%	NS

¹ One male patient (of 59) and one female patient (of 65) were not fully examined for technical reasons.

² Chi square 7.29, corrected chi square 5.54.

³ Chi square 3.92, corrected chi square 2.60.

confidence interval 1.3 – 45.3), and of a cardiovascular disease (stroke, myocardial infarction and/or symptomatic heart diseases) to 4.3 (95% confidence interval 1.7 – 10.1).

Cohort study

It is seen from table IV that both the systolic and the diastolic blood pressures were considerably higher ($p < 0.01$) in the subcohort of pensioners with hypertension compared with the subcohort of pensioners without hypertension at the age of 70 years; the mean difference in 1971/1972 being 35/12 mm Hg in males and 32/10 mm Hg in females.

The difference in systolic blood pressure between the two subcohorts remained during the study. In 1978/1979 ($n_1 = 28$ and $n_2 = 72$) the systolic blood pressure (mean $\pm$ SEM) was 175 ± 3.8 and 163 ± 2.8 , respectively, ($p < 0.05$). There was no difference in the diastolic blood pressure between the two subcohorts in 1978/1979. In 1978/1979 the diastolic blood pressure (mean $\pm$ SEM) was 90 ± 2.1 and 86 ± 1.3 , respectively.

The mean systolic and diastolic blood pressures in hypertensive male pensioners in this study in 1971/

1972 (Table IV) was higher ($p < 0.001$ and $p < 0.05$) than in hypertensive patients in the retrospective study in 1981 (Table I). In females the results were similar ($p < 0.01$ for the systolic and $p < 0.05$ for the diastolic blood pressure).

Heart rate (mean $\pm$ SEM) in 1971/1972 was higher ($p < 0.001$) in pensioners with hypertension (81 ± 3.5) compared with pensioners without hypertension at the age of 70 years (71 ± 1.2). A significant difference remained during the study.

Of all the hypertensive patients in the study in 1971/1972 ($n = 39$) 54% were treated with one antihypertensive drug and ten % with two drugs. Thirty-six % were not treated with any antihypertensive drug. In 1981/1982 ($n = 31$) 58 % were treated with one antihypertensive drug, ten % with two and six % with three antihypertensive drugs. Twenty-three % were not treated with any antihypertensive drug.

In the subcohort of hypertensive pensioners ($n = 39$) 342 person-years were studied (121 in males and 221 in females). In the subcohort of pensioners without hypertension at the age of 70 ($n = 105$) 890 person-years were studied (548 in males and 342 in females). In table V the mortality rates of the two subcohorts are shown as well as the relative risk of

Table IV. Blood pressure during treatment, mean $\pm$ SEM (mm Hg) in male and female hypertensive pensioners (Ht) born in 1902 and 1903 who reached the age of 70 in comparison with pensioners without hypertension at that age (NHt). P indicates the level of significance.

Sex	Numbers and blood pressure	1971/1972		
		Ht	NHt	p
Male	(n)	(14)	(63) ¹	
	systolic	184 ± 5.1	149 ± 2.3	< 0.001
	diastolic	98 ± 4.3	86 ± 1.3	0.001
Female	(n)	(24) ²	(36) ³	
	systolic	182 ± 6.2	160 ± 3.2	0.001
	diastolic	97 ± 2.3	87 ± 1.7	< 0.01

¹ 5 cases not attending

² 1 case not attending

³ 1 case not attending

Table V. Mortality rate in a cohort of pensioners born in 1902 and 1903 and living in Dalby Primary Care district dichotomized into those with hypertension (Ht) and those without (NHt) at the age of 70 years.

Group	Deaths per 1000 person-years	Relative risk of death
NHt	39.4	1
Ht	26.3	0.67 ¹

¹ 95 per cent confidence interval 0.27–1.42

death. No difference in the death rates for either sex in the two subcohorts was found (chi square below 0.25).

In figure 3 the survival rates of the two subcohorts are shown for men and women separately. In figure 4 the survival rate of the non-attending pensioners in 1969/1970, who reached the age of 70, is shown for men and women separately. No difference between attending and non-attending pensioners of the same sex was found.

In the subcohort of hypertensive pensioners nine died during the study. Autopsy was performed in seven of them (78 %). Six died of cardiovascular diseases, two of malignant neoplasms and one of an infectious disease. In the subcohort of pensioners without hypertension at the age of 70, 35 died during the study. Autopsy was performed in 29 (83 %) of them. Twenty-seven died of cardiovascular diseases, five of malignant neoplasms, two of infectious diseases and one of uremia.

In the 34 pensioners not attending the first examination in 1969/1970, four died before and nine at the age of 70 years or thereafter. Autopsy was performed in

nine of them (69 %). Eight died of cardiovascular diseases, one before and seven at the age of 70 years or thereafter. Five died of malignant neoplasms, three before and two after the age of 70 years. There were no differences in the death rates when the non-attendants, who reached the age of 70 years ($n = 30$) were compared with the pensioners in the two subcohorts (chi square below 0.5).

Autopsy was performed in ten (83 %) of the twelve pensioners who died between the age of 67 and 70 and who were not included in the cohort. Nine died of cardiovascular diseases and three of malignant neoplasms. Two had a diagnosis of hypertension in their medical records and another two had diabetes.

In table VI the cumulative incidence rates of stroke, symptomatic heart diseases, myocardial infarction and diabetes during the study are listed for both sexes together as well as the relative risk of these diseases in the two subcohorts. No significant difference in the occurrence of stroke, symptomatic heart diseases, myocardial infarction nor diabetes was found between the two subcohorts (chi square below 1.5). The occurrence of cardiovascular complications

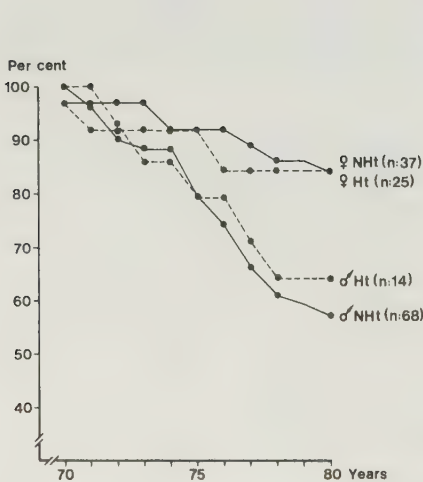


Fig. 3. Survival rate of male and female pensioners born in 1902 and 1903, who reached the age of 70 years and had the diagnosis of hypertension (Ht) in comparison with pensioners without hypertension at that age (NHt).

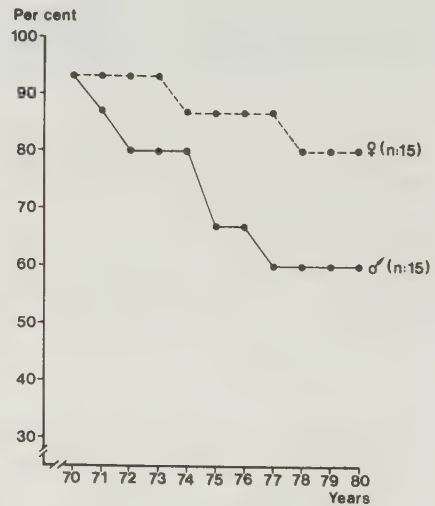


Fig. 4. Survival rate of male and female non-attendant pensioners born in 1902 and 1903 who reached the age of 70 years ($n = 30$).

Table VI. Ten year cumulative incidence rates of stroke, symptomatic heart disease, myocardial infarction and diabetes in a cohort of pensioners born in 1902 and 1903 dichotomized into those with hypertension (Ht) and those without (NHt) at the age of 70 years.

Disease group		Cumulative incidence rate per 1000 person-years	Relative risk	Attributable risk per 1000 person-years
Stroke	{ NHt	12.4	{ 1	8.1
	{ Ht	20.5	{ 1.7	
Symptomatic heart disease	{ NHt	29.2	{ 1	5.9
	{ Ht	35.1	{ 1.2	
Myocardial infarction	{ NHt	16.9	{ 1	6.5
	{ Ht	23.4	{ 1.4	
Diabetes	{ NHt	6.8	{ 1	2.0
	{ Ht	8.8	{ 1.3	

did not differ when non attending pensioners were compared with attending pensioners (chi square below 3.3).

In the subcohort without hypertension at the age of 70 years ($n = 105$) 12 pensioners (six males and six females) got the diagnosis hypertension after the age of 70. Three of them (25 %) died during the study compared with 32 (34 %) of the pensioners without hypertension. This difference was not significant (chi square below 0.1).

DISCUSSION

Hypertension is a common condition in primary health care. In 1980 hypertension was second only to diabetes among the most common diagnoses at the Dalby Health Care Centre in the age group 65–74 years and accounted for 19 % of all consultations in this age group ($n = 1981$).

In the year 1981 the prevalence of hypertension was estimated to at least 18.8 % (including newly diagnosed hypertension 1.4 %). Antihypertensive drugs were given to 93 % of the known hypertensives. The prevalence of hypertension was of course highly influenced by the blood pressure limits used for diagnosis of hypertension and borderline hypertension. The prevalence of borderline hypertension was at least 13.7 % (including newly diagnosed borderline hypertension 8.7 %). Our figures compare well with the prevalence of treated hypertension in the county of Skaraborg in Sweden in 1977, for the age 65 years, 16.7 % of males and 24.8 % of females or in total 20.8

% (10). These results may be compared with the prevalence figures reached when the WHO recommendations for diagnosis of hypertension are used, e.g. 50 % in the United States National Health Survey (11).

One of the aims of this study was to describe hypertension in the elderly as it appears in primary health care. In the retrospective study performed in 1981 the medical examinations were highly standardized as described in the section on methods. The blood pressure reached during treatment, mean $\pm$ SEM (mm Hg) was, $160 \pm 2.3/92 \pm 1.1$ for males and $165 \pm 2.2/91 \pm 1.2$ for females, and thus considerably lower ($p < 0.001$) than before treatment. The agreed goal of treatment of hypertension in patients aged 60 – 69 years in the county of Malmöhus in Sweden, i.e. 180/100 mm Hg or below, was reached by 76 % of the male patients and 75 % of the females. This indicates, that primary health care is capable of handling hypertension. However, in comparison with the non-hypertensive controls the blood pressure during treatment was considerably higher ($p < 0.001$) and still with mean values above the systolic blood pressure limits for hypertension according to WHO. In comparison with other studies, e.g. EWPHE (European Working Party on High Blood Pressure in the Elderly) sixth interim report in 1980 (12), our figures during treatment are approximately 15/10 mm Hg higher but our before-treatment values were approximately 20/15 mm Hg higher as well.

In a study by Simpson in New Zealand (13) on hypertensive patients aged 65 or more and with a

degree of fatness ($w/h^2 = 27.3$) comparable with our study ($w/h^2 = 28.0$ for males and 29.5 for females), blood pressure before treatment averaged 190/106. The level achieved with therapy averaged 159/90. It is interesting that our study as well as that from New Zealand, which both comprise patients from primary health care, achieved the same blood pressure reductions. Probably this represents what family physicians find feasible in patients of this age group.

The population in our primary care district in the age group 60–69 years was characterized by an overweight in females ($w/h^2 \geq 25$) and a normal degree of fatness in males ($w/h^2 < 27$). Hypertensive patients, female as well as males, were overweight (w/h^2 29.5 and 28.0, respectively). The population is also characterized by the alcohol and smoking habits of the inhabitants. Our attending control group comprised 84 % of the sample. Of course, there may be a hidden abuse of alcohol as well as tobacco in the group of non-attendants. This will, however, hardly affect the comparison of alcohol habits between patients and controls. Our results indicate no differences in alcohol habits between patients and controls in this study of elderly people, living in a suburban and rural area. This conclusion is supported by serum glutamyl transferase (S-GT) values well within the normal limits for both groups and without significant differences. A positive correlation between high blood pressure and alcohol has been described in other studies (14–16) but they have mostly comprised young or middle aged persons often living in large cities.

Smoking was less frequent in female patients compared with their controls ($p < 0.05$). This was not the case in men. The percentage of ex-smokers did not differ between the groups in either sex. This means that it was not advice given in the consulting room which might explain the difference in female smokers in our study.

In this retrospective study documented data regarding cerebrovascular diseases were more common ($p < 0.05$) among male hypertensive patients than among their controls. This was also the case, when all cardiovascular events were considered together in males (chi square 11.11, $p < 0.01$). The corresponding figures for females did not differ, which may depend on the small material. However, uncorrected chi square indicated a low degree of significance in differences between female patients and their controls regarding symptomatic heart diseases. This difference was not significant after Yates' correction. The-

re were no differences between female patients and their controls, when all cardiovascular events were considered together (chi square 2.33).

As disease-rates are not obtained directly in a study like this relative odds can only be estimated (17). However, the controls were representative of the total population in this age group, in spite of their being matched to the age distribution of the patients. It may be considered that the variation in frequency of diseases within this age group (60–69 years) is small. Our patients represent a sample of all known hypertensives in a defined population in this age group. They are selected in a known way and represent about 85 % of the (known) total hypertensive population. They do not differ from the small group of hypertensives (15 %) taken care of by other physicians. This retrospective study in primary health care has shown, that hypertensive males at the age of 60–69 years have a chance of stroke 7.7 (1.3–45.3) times more often than their non-hypertensive controls. Our data are collected in a group of male patients, where more than 90 % were treated with antihypertensive drugs. However, our study design does not allow any conclusions to be drawn regarding the effect of drug treatment on these risks.

The Framingham study (2) demonstrated that hypertension was important risk factor for cardiovascular disease, notably coronary heart disease, heart failure and stroke at all ages. Among subjects of both sexes between 65 and 74 years old, those with hypertension had an annual incidence of cardiovascular disease three times greater than normotensive persons. The EWPHE study (12) which is specially designed to evaluate the potential benefits of antihypertensive treatment has not yet reported results regarding morbidity in elderly patients on active treatment compared with placebo.

The cohort study of all pensioners born in 1902 and 1903 in a defined population was performed in order to use longitudinal data in the evaluation of morbidity and mortality of hypertension in those above the age of 70 years. It may be underlined, that data on morbidity and mortality were also analysed on non-attendants, thereby compensating for the small material. The subcohort of pensioners with a diagnosis of hypertension at the age of 70 was characterized by considerably higher blood pressure in comparison with the non-hypertensive subcohort. During an observational period of seven years pensioners in the hypertensive subcohort kept their high systolic blood pressure level. This was still significantly higher ($p < 0.05$)

than the corresponding value in the non-hypertensive subcohort after seven years, in spite of the fact that the systolic blood pressure in the latter group had risen ($p < 0.01$). Diastolic blood pressure was higher ($p = 0.001$ in males and < 0.01 in females) in the hypertensive subcohort at the age of 70 compared with the non-hypertensive subcohort. This difference disappeared during the observational period depending on a fall in diastolic blood pressure in the hypertensive subcohort ($p < 0.05$).

The hypertensive pensioners at the age of 70 had significantly higher blood pressure values—systolic and diastolic—than the hypertensive patients in the retrospective study at the mean age of about 65 years.

The hypertensive pensioners in the cohort study were to a less degree treated with antihypertensive drugs than the patients in the retrospective study.

The relative risk of death was 0.67 (0.27 – 1.42) in the subcohort of hypertensives compared with non-hypertensives. The autopsy protocols and death certificates did not show any differences in cardiovascular death between the subcohorts. There were relatively low excess risks (1.2 – 1.7) and attributable risks (2.0 – 8.1) for the occurrence of stroke, symptomatic heart diseases, myocardial infarction and diabetes in the subcohort of hypertensives during the ten year observational period.

The results are presented for both sexes together in table VI because of the small material. If, however, the results were looked upon separately the relative risks for the occurrence of stroke and symptomatic heart diseases were 3.9 (0.8 – 18.7) and 2.2 (0.7 – 8.2) in female hypertensives. The corresponding figures in male hypertensives were 1.0 and 1.1. There were no differences between the sexes in the occurrence of myocardial infarction.

Regarding morbidity our data from the retrospective study of 60 – 69 year old hypertensive patients and their controls, and our ten year prospective cohort study of all pensioners aged 70 – 80 years have shown higher relative risks for males below the age of 70 as compared with above the age of 70. This is the case in spite of the latter group being older, having higher systolic blood pressure at the examinations and having less degree of antihypertensive drug treatment. Of course the difference in risks in the two age groups could be influenced by the design, comparing a retrospective study with a prospective cohort study. However, analysis of the two materials has not pointed at confounding factors or bias in the selection procedures affecting the results. Obviously the difference can

be attributed to a selection process with greater survival and less morbidity among those who reach the age of 70. In a study from Scotland, Anderson and Cowan (18) showed that systolic and diastolic blood pressures were of no predictive value in estimation of survival time in a group of healthy men and women aged 70 years or more. Fry (19) found in a study from a London general practice of the natural history of hypertension, an observed/expected death ratio in untreated hypertensives of 1.15 in the age group 60 – 69 years and of 0.87 in the age group 70 years or more. His conclusion was, that the risks of life with high blood pressure vary with the age at which hypertension was first observed, and that over the age of sixty there seemed to be no extra risk of death for (untreated) hypertensives. Our retrospective study of patients aged 60 – 69 years and their non-hypertensive controls says nothing about death rates, but our ten year prospective cohort study of treated hypertensives aged 70 – 80 years indicates results similar to those of Fry's. Against this background it is essential to study the benefits of drug treatment of hypertension above the age of 70 years.

ACKNOWLEDGEMENTS

This work was supported by grants from the National Board of Health and Social Welfare in Sweden. We express our thanks to Professor em. Åke Nördén and to Dr Gustav Haglund for giving us access to data from the prospective studies of pensioners in Dalby.

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PARENTAL OBESITY COMBINED WITH HYPERTENSION -
AN INDICATOR OF EXCESS RISK OF HYPERTENSION IN OFFSPRING

A Case-control Study in a Swedish Primary Care District

by

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ABSTRACT

A case-control study was performed to estimate the excess risk of hypertension in a defined population. The study comprised 121 hypertensive patients aged 40-59 years and 138 non-hypertensive controls, selected from the same primary care district.

Parental obesity combined with hypertension proved to be a stronger risk indicator of hypertension in offspring than was parental hypertension itself. Other risk indicators were obesity, hypertension in siblings and a positive family history of myocardial infarction.

In order to study the size of the problem we estimated the prevalence of hypertension and borderline hypertension in the district. Patients with these diagnoses amounted to about one-fourth of the middle-aged population in the district. More than 80 % of the hypertensives had been diagnosed before this study, but only about 20 % of the borderline hypertensives were previously known.

Keywords: Hypertension, epidemiology, risk, primary health care, family history, obesity

INTRODUCTION

It is well established that first-degree relatives resemble each other as regards blood pressure (1) and it is also well known that high blood pressure runs in families and that some of the relatives of patients with hypertension are likewise hypertensives (2). The extent to which hypertension is genetically determined is still a matter of controversy, however, as also is the possible contribution of environmental factors. Assessment of the family history of hypertensives is important, both to gain an understanding of the patients' fears and expectations and to create a motivation for treatment and follow-up (3).

Hypertension and obesity are two common, interrelated health hazards (4). Family factors may well be of importance for the development of obesity in childhood, but as the individual grows older, the environment becomes increasingly important. Hypertension is more common in the obese than among the non-obese. Conversely a significant proportion of hypertensives in a population is overweight (5-7).

Obese hypertensives run a greater risk of developing cardiovascular diseases than do non-obese (5). Weight reduction has been shown to lower blood pressure (8) and may bring about a more favourable prognosis in obese hypertensives (4). The long-term effectiveness of reducing calorie consumption in hypertensives has yet to be demonstrated, however.

We have found a high odds ratio of cardiovascular diseases in earlier studies on well-treated male hypertensives compared with non-hypertensive controls (9-10). This was the case even though the patients' blood pressure had been reduced in accordance with internationally accepted norms and 75 % of the patients had achieved their treatment objective. We also found a positive partial correlation between blood pressure group and body mass index (w/h^2 , kg/m²) even though instructions regarding diet and calorie reduction had been given to the hypertensives - when indicated (10).

Against this background we found it interesting to analyse the excess risk of hypertension in middle-aged persons with a positive family history of obesity, hypertension or cerebro-cardiovascular diseases as well as to estimate the size of the problem in a defined population in primary health care.

The purposes of this study were:

- to investigate the prevalence of hypertension in middle-aged males and females in a primary care district
- to analyse the relative odds (risk) of hypertension in obese persons
- to analyse the relative odds of hypertension in persons with a positive family history of obesity, hypertension, myocardial infarction or stroke.

METHODS AND STUDY POPULATION

Study population

The study population has been described in detail elsewhere (10). In summary, all patients born in the period 1922-41 who visited the Dalby Health Care Centre in 1980 because of actual or borderline hypertension ($n = 156$) were invited to a medical examination in 1981 including a structured interview and various laboratory tests. Their representativity of the defined population was documented. Of these patients 152 (97 %) attended the examinations. They were divided into two groups - hypertensives and borderline hypertensives - according to the diagnosis in their medical records based on criteria described below. They were compared with an age- and sex-matched control group from the same primary care district, chosen with the aid of the official population register. All inhabitants in the primary care district are recorded in this register in chronological order. For each patient who attended the medical examinations, persons of the same sex located before and after the patient in the population register were selected as controls. In this way 295 persons born the same year and month as the patients - and mostly even on the same day - formed the control group, of whom 244 (83 %) attended.

Controls who had a diagnosis of hypertension or borderline hypertension as well as those who had a systolic blood pressure exceeding 155 mm Hg, or a diastolic blood pressure exceeding 90 mm Hg, at either of two examinations were not included in the analyses. Altogether 73 control persons were thus excluded.

Only the hypertensive cases ($n = 121$) and their controls ($n = 138$) were considered in this study. All comparisons were made between the group of patients and the control group.

Organization

Patients and controls were first interviewed by a single, specially trained nurse concerning their family history of cerebro-cardiovascular diseases and hypertension. The family history of hypertension was considered positive if a person had a parent or a sibling who attended a doctor or a nurse because of high blood pressure and was otherwise categorized as negative or uncertain depending upon the answer. Blood pressure, weight (w , kg) and height (h , m) were recorded by the nurse and the body mass index (w/h^2) was calculated. All cases and controls were then seen by a physician who made a conventional clinical examination. Anamnestic data including past history of diseases were recorded at a structured interview.

After the examinations, all cases and controls ($n = 259$) were mailed a questionnaire in which they were asked to rate their parents as very fat, fat, normal, thin or very thin when middle-aged. The questionnaire was returned by 238 persons (92 %).

Validity of questionnaire

The validity of the questionnaire was examined in a group of 40 cases (hypertensives) and controls (non-hypertensives). The youngest ones were chosen, as their parents were in most cases below 70 years of age. These cases and controls were mailed a second questionnaire (after having answered the first one) in which they were asked to state their parents' present age, weight and height. The parents were asked to consult their local district nurse to have accurate measurements taken. The second questionnaire was returned by 39 persons (98 %) and information was obtained about 37 mothers (93 %) and 28 fathers (70 %). Altogether 62 parents out of 65 were graded as either fat or having normal weight. Thus, only two categories of the scale were used. The results of the validity study in both parents are shown separately for patients and controls in Figure 1.

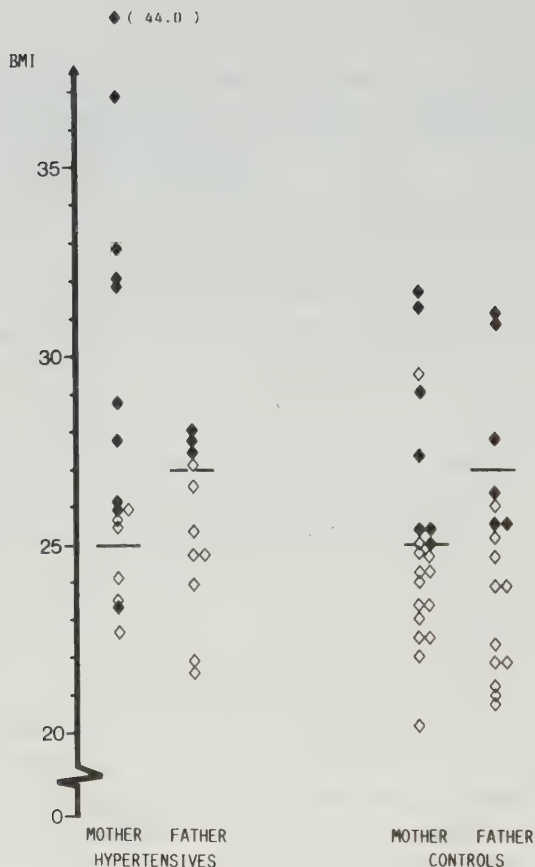


Figure 1. Body mass index (BMI) in parents, related to body weight estimated by their offspring (hypertensives and controls) as obese $\blacklozenge$ and non-obese $\lozenge$.

Body mass index (mean $\pm$ SE) was higher ($p < 0.001$) in parents categorized as fat (28.7 ± 0.98) in comparison with parents categorized having normal weight (24.5 ± 0.39). The difference was significant in both sexes. In the further analyses parents have been categorized as either obese (including fat and very fat, according to the scale) or non-obese (including normal, thin and very thin). Cases and controls were categorized according to their body mass index (BMI) as either obese (BMI: males ≥ 27 , females ≥ 25) or non-obese (11).

Criteria for diagnoses of hypertension and borderline hypertension

At the Health Care Centre in Dalby the blood pressure limits used in the daily routine for asymptomatic patients aged 40-59 years were (mean of at least three measurements): for hypertension > 170/> 105 mm Hg, and for borderline hypertension 160-170/95-105 mm Hg. If the patients had diabetes the limits were 5-10 mm Hg, lower.

Non-attending patients and controls

Information has been obtained about all non-attending patients and 76 % of the non-attending controls, as described elsewhere (10). We have no information about the non-attenders' parents but see no reason why they should differ from those of the attenders.

Prevalence of hypertension and borderline hypertension

The prevalence of hypertension was estimated for the age groups 40-49 and 50-59 years from the number of hypertensives found in the control material. The corresponding figures for borderline hypertension were estimated in the same way. The annual prevalence was weighted according to the formula:

$$\text{Prevalence} = \frac{\sum N_i \times \frac{h_i}{n_i}}{\sum N_i}$$

where h_i was the number of hypertensives at i years of age. N_i and n_i were the corresponding numbers of individuals in the population (N_i) and sample (n_i). Thus h_i/n_i was the prevalence at age i . Since the prevalence of hypertension increased with age, the older ages were over-represented in the control material, depending on the method of selection. The estimate of hypertension would have been too high if the weighting had not been performed. The effects of the increase in the prevalence within each year were small and therefore ignored.

Data processing and statistical methods

All data were analysed with the SPSS Program System on a Univac Computer (1100/80). Student's t -test (two tailed) was used to test the hypothesis of no difference in mean value between two groups. In order to test the difference between frequencies in two groups, the Chi-square test was used. Yates'

correction for continuity was applied where any of the expected frequencies was less than five for one degree of freedom. Statistical significance was evaluated at the levels $p < 0.05$, < 0.01 and < 0.001 . A difference was considered significant when the p-value was < 0.05 .

The relative odds - i.e. the ratio of affected to unaffected individuals in one group **with** a certain characteristic divided by the same ratio in another group **without** that characteristic - were estimated and corrected for small numbers, and the 95 % confidence limits were estimated as recommended by Lilienfeld (Haldane's method), (12).

RESULTS

The prevalence of hypertension (both sexes) was estimated to at least 4.4 % in the age group 40-49 years and 14.8 % in those aged 50-59 years. The corresponding figures for borderline hypertension were 11.4 and 12.5 %, respectively.

Most hypertensives were diagnosed before the examinations (4.4 % in the age group 40-49 years and 11.9 % in those aged 50-59 years). Few borderline hypertensives had been diagnosed previously (2.8 % in the age group 40-49 years and 2.4 % in those aged 50-59 years). There were no differences between the sexes.

Hypertensives of both sexes had higher ($p < 0.001$) body mass index (BMI) than their controls. In males, BMI (mean $\pm$ SE) amounted to 28.4 ± 0.4 and 25.0 ± 0.3 respectively and in females to 28.1 ± 0.7 and 25.2 ± 0.5 .

The corrected odds ratio of hypertension in males with vs. without obesity was estimated to 5.4 (95 % confidence interval 2.6-11.2) and in females to 2.5 (1.2-5.3) (Table I).

When the degree of obesity in fathers and mothers was rated by the patients and controls, no tendency of assortative mating (13) was found (Table II). There was no tendency to rate both parents obese more often than expected.

Table I. Relative odds of hypertension, (ψ_c) in males and females aged 40-59 years, with vs. without obesity.
Ht: hypertensives; NHt: non-hypertensives; (95%): 95% confidence interval

	Males			Females		
	Cases (Ht)	Controls (NHt)	Rel. odds ¹ ψ_c (95%)	Cases (Ht)	Controls (NHt)	Rel. odds ¹ ψ_c (95%)
Obese	41	17	5.4 (2.6-11.3)	36	27	2.5 (1.2-5.2)
Non-obese	25	58		19	36	

¹ corrected for small numbers.

Table II. Test of assortative mating regarding obesity in fathers and mothers, as rated by cases and controls

	Numbers		
	Obese mother	Non-obese mother	Total
Obese father	27	41	68
Non-obese father	71	70	141
Total	98	111	209

$$\chi^2 = 2.1 \text{ d.f.} = 1 \text{ N.S.}$$

There was a significant excess risk of hypertension in males with obese and hypertensive parents and also in females with obese and hypertensive mothers (Table III). This was not so either in males or in females with hypertensive but non-obese parents.

Table III. Relative odds of hypertension, (ψ_c) in males and females aged 40-59 years, with regard to obese and non-obese parents, with vs. without hypertension.

Ht: hypertensives; NHt: non-hypertensives; (95%): 95% confidence interval

	Males			Females		
	Cases (Ht)	Controls (NHt)	Rel odds ¹ ψ_c (95%)	Cases (Ht)	Controls (NHt)	Rel odds ¹ ψ_c (95%)
Mother obese						
Ht	19	3	8.0 (2.1-30.6)	14	6	4.4 (1.3-14.3)
NHt	13	19		10	20	
Mother non-obese						
Ht	7	5	2.3 (0.7-7.8)	6	6	1.5 (0.4-5.4)
NHt	23	40		15	23	
Father obese						
Ht	10	2	6.1 (1.3-27.9)	2	1	2.6 (0.3-23.6)
NHt	15	22		7	11	
Father non-obese						
Ht	4	0	14.1 (0.7-270)	7	3	2.9 (0.7-11.2)
NHt	28	44		26	35	

¹ corrected for small numbers.

There was a significant excess risk of hypertension in males and females with hypertensive siblings (Table IV) as well as in males with a positive family history of myocardial infarction in fathers or in siblings (Table IV).

DISCUSSION

In this study we have considered the problem of excess risk of hypertension in middle-aged persons in a defined population, particularly focusing on those with parental obesity combined with hypertension. We have also estimated the size of the problem by analysing the prevalence of hypertension as well as borderline hypertension in our primary care district.

The prevalence of hypertension, according to the criteria given above, was estimated to at least 4.4 % in the age group 40-49 years and at least 14.8 % in those aged 50-59 years. Most hypertensives were diagnosed before the exam-

Table IV. Relative odds of hypertension, (ψ_c) in males and females aged 40-59 years, with hypertensive vs. non-hypertensive siblings, or a positive vs. negative family history of myocardial infarction or stroke. Ht: hypertensive; NHt: non-hypertensive; MI: myocardial infarction; S: stroke; (95%): 95% confidence interval

	Males			Females		
	Cases (Ht)	Controls (NHt)	Rel odds ¹ ψ_c (95%)	Cases (Ht)	Controls (NHt)	Rel odds ¹ ψ_c (95%)
Sibling						
Ht	18	5	5.0 (1.8-14.0)	13	3	6.5 (1.9-22.6)
NHt	43	64		32	54	
Mother						
MI	8	5	1.9 (0.6-5.8)	6	3	2.3 (0.6-8.8)
no-MI	58	70		49	60	
Father						
MI	12	5	2.9 (1.02-8.5)	10	6	2.0 (0.7-5.8)
no-MI	54	70		45	57	
Sibling						
MI	14	4	4.4 (1.4-13.6)	2	3	0.9 (0.2-4.8)
no-MI	47	65		43	54	
Mother						
S	9	5	2.1 (0.7-6.4)	12	11	1.3 (0.5-3.2)
no-S	57	70		43	52	
Father						
S	11	9	1.5 (0.6-3.7)	7	6	1.4 (0.4-4.2)
no-S	55	66		48	57	
Sibling						
S	3	1	2.7 (0.4-19.1)	3	0	9.5 (0.5-189)
no-S	58	68		42	57	

¹ corrected for small numbers

inations. However, our study has also shown a prevalence of borderline hypertension of about 12 % in both age groups, of whom very few were known beforehand. These figures are in accordance with what has been published in studies from the County of Skaraborg in Sweden (13). They should be considered when discussing screening, treatment and follow-up of middle-aged patients with mild or borderline hypertension, since together they amount to about one fourth of the middle-aged population in the primary care district.

It has been found that about 75 % of the adult population (20 years old or above) in our primary care district have visited the Health Care Centre at some

time during a five-year period, 1975-79 (15). More than half of the adult population have had their blood pressure recorded at the Health Care Centre during this period. About 65 % of all inhabitants in the district visit the centre each year, which accords with what has been published internationally (16). These figures indicate the realistic possibility of screening the population for high blood pressure within the regular consulting routine of a health care centre. The long term effectiveness of such a program, however, has yet to be demonstrated.

Another way to diagnose unknown hypertension, is to screen those in the population who have risk indicators of hypertension. This study points out three risk indicators: obesity, parental hypertension combined with obesity, and a family history of myocardial infarction.

Our hypertensives were more obese than their controls. About two-thirds of the male and female cases were obese when examined in comparison with about one-third of the controls.

The odds ratio (corrected for small numbers) of hypertension in the obese was estimated to 5.4 (2.6-11.2) in males and 2.5 (1.2-5.3) in females. This may be compared with the Framingham study (6) where the risk of hypertension in previously normotensive individuals was proportional to the degree of overweight. Hypertensives also had an increased tendency to develop obesity. Kannel concluded "that adiposity predisposes and makes a significant contribution to development of hypertension in adult men and women beyond age 30" (6). This has been confirmed in large studies comprising more than a million people (17).

It is therefore interesting to note that studies on limited numbers of cases and controls in a defined population in primary health care analysed in this way give results which are comparable to studies made on large populations.

A positive family history of hypertension is one of the most established risk indicators of this disorder. In our case-control study about 42 % of the male and 44 % of the female patients reported maternal hypertension in comparison with 12 and 21 % respectively of the (non-hypertensive) controls (Table III). Paternal hypertension was reported by 25 % of the male and 22 % of the female patients, in comparison with 3 % and 8 % respectively of the controls (Table III). Our results compare well with studies on middle-aged males in Malmö (personal communication, 18) where the overall frequency of hypertension in a first degree relative was about 26 %. Maternal hypertension was twice as common as paternal in the Malmö study, which is similar to our results.

We have obtained information about the family history of hypertension and cardiovascular diseases by means of a structured interview. This was done in a way similar to that in current clinical practice. The patients may be more aware of cardiovascular diseases and hypertension in their relatives since they are hypertensives themselves in contrast to the controls who mostly are healthy. It has been shown, however, that middle-aged males' knowledge of their parents' diseases and cause of death is reliable and can be used for therapeutic purposes in familial disease (19).

In our study all patients and controls were interviewed in the same way and by the same nurse. Great care was taken to obtain accurate information. The family history of hypertension was categorized as "positive" only if a person claimed a first-degree relative to have consulted a doctor or a nurse because of high blood pressure. Otherwise, it was categorized as "negative" or "uncertain". There was no significant difference in the frequencies of "uncertain" answers between the groups.

When the relative odds of hypertension were estimated in individuals with parental hypertension, we also considered the parents' degree of obesity, since there is a familial clustering of these variables (5-7). A high degree of validity of our estimates of parental obesity was found (see Methods and Fig. 1).

We have shown that a combination of obesity and hypertension in the parents tallies with a significant excess risk of hypertension in their offspring (Table III). This was not so in those with parental hypertension without obesity.

To avoid a type II fallacy it should be emphasized that this difference between the groups may be explained by the limited numbers in our study. However, although all results point in the same direction (excess risk) three of four reach significance in the former group whereas no results reach significance in the latter. This indicates that parental hypertension together with obesity is a stronger risk indicator of hypertension in offspring than is parental hypertension itself.

We have not found any study which distinguishes obese from non-obese parents in the analyses of familial aggregation of hypertension in adults, though, studies in adolescents have shown that familial blood pressure resemblances are not explained solely by familial similarities in body weight (20). Our results show hypertension in siblings to be a risk indicator of hypertension in males as well as in females (Table IV). There was also an excess risk of hypertension in males

with a positive family history of myocardial infarction in fathers and siblings (Table IV).

A positive family history of stroke was not shown to be a significant risk indicator of hypertension in this study, although this may be due to the limited numbers. Others have shown (21) that middle-aged men with a cardiovascular risk profile have parents and siblings with increased cerebro-cardiovascular morbidity and mortality. In a community health survey in Reykjavik (22) the group with a positive family history of stroke had a mean systolic blood pressure 10 mm Hg, higher than the negative group, thus motivating a blood pressure screening of first degree relatives of patients with stroke.

The question whether a positive family history of cerebro-cardiovascular disease is an independent risk indicator or whether it acts together with hypertension and/or diabetes has still to be answered, however.

To conclude, our study has demonstrated a combination of parental obesity and hypertension as being a stronger risk indicator of hypertension in offspring than is parental hypertension itself. We have also found obesity, hypertension in siblings and a positive family history of myocardial infarction to be risk indicators of hypertension. How these findings can be utilized in the diagnosis of unknown hypertension in a primary care district, and whether they have any bearing upon borderline hypertension, merit further studies.

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IMPACT OF HYPERTENSION ON A DEFINED POPULATION:
UTILITY OF A POPULATION-BASED CASE-CONTROL
STUDY MODEL OF LIMITED NUMBERS
IN ESTIMATING RISKS

by

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SUMMARY

The 10-year incidence of myocardial infarction and stroke in subjects below 70 years of age was used to analyse the usefulness of a population-based case-control study model in a small primary care district, where extensive studies and treatment programs regarding blood pressure have been performed during the last decade.

The results showed hypertension and smoking to be independent risk indicators of myocardial infarction and hypertension to be a strong risk indicator of stroke in males. The impact of hypertension on the male population below the age of 70 years was 30 % with regard to myocardial infarction and 68 % to stroke. Our results are in agreement with those obtained in large and prospective studies and may be considered to express the degree of benefit of the antihypertensive care program in the district.

Thus, a limited number of patients in a defined population can be utilized in epidemiological studies regarding risk and can therefore justify this model for studies in primary health care.

INTRODUCTION

In primary health care the number of people in each catchment district is limited. This necessitates the use of research models that can be applied to small groups of people and yet give valid results. Another way to overcome the problem of small numbers is of course to use a multicentre research technique, though this would entail the disadvantage of involving many investigators.

We found it of interest to analyse whether a limited group of patients, below the age of 70 years and representing all known cases of cerebro-cardiovascular disease (CCVD) during a 10-year period in a primary care district, could be utilized for studies on the impact of hypertension on the population, regarding this disease.

Hypertension has a prevalence of about 15 % in the middle-aged males in our district, as described elsewhere (1,2). If borderline hypertension is included, the prevalence increases to about 25 %.

High blood pressure is a serious risk indicator of CCVD and mortality in middle-aged males, especially if other indicators such as smoking and/or a high cholesterol level are also present (3-5). Lowering of high blood pressure is an effective way of reducing morbidity and mortality in both established and mild hypertension (6-9).

Smoking is also a risk indicator of cardiovascular disease (4,5,10,11) and some studies have indicated that discontinuing smoking reduces the risk of ischaemic heart disease (12).

We have found a high risk of CCVD in hypertensive males, even though their blood pressure was reduced in accordance with internationally accepted recommendations and their smoking habits had been reduced as well (1,13). Compared with non-hypertensive controls, however, the hypertensives' blood pressure was still at least 10-15 mm Hg higher, and their degree of obesity considerably higher. In view of these findings, we considered it of interest to analyse the impact of hypertension and smoking on the population influenced in this way for almost 15 years. We have used the incidence of myocardial infarction and stroke to analyse the usefulness of a population-based case-control study model.

Cases

All new cases of myocardial infarction and stroke born between 1912 and 1931 and diagnosed during the period 1973-82 among the inhabitants of the Dalby primary care district (21,000) were identified by means of the statistical computer system for in-patient care in the County of Malmöhus (500,000 inhabitants) as well as the out-patient care scheme in the Dalby primary care district. These schemes can be described as individually based computer systems for the processing of statistical information about patients and their contacts with the health and medical care services. They have been described in detail elsewhere (14,15). The in-patient scheme gathers information from all hospitals in the County of Malmöhus regarding patients admitted. The Dalby out-patient scheme gathers information from the health care centres in Dalby and Sandby. In both schemes the patients were registered by their civic registration numbers and the diagnoses according to the ICD (International Statistical Classification of Diseases) codes (16). Myocardial infarction and stroke were identified by ICD codes 410 and 430-438 respectively. The numbers of patients identified in the two schemes were compared in Figure 1. There was no clustering of cases within the ten-year period.

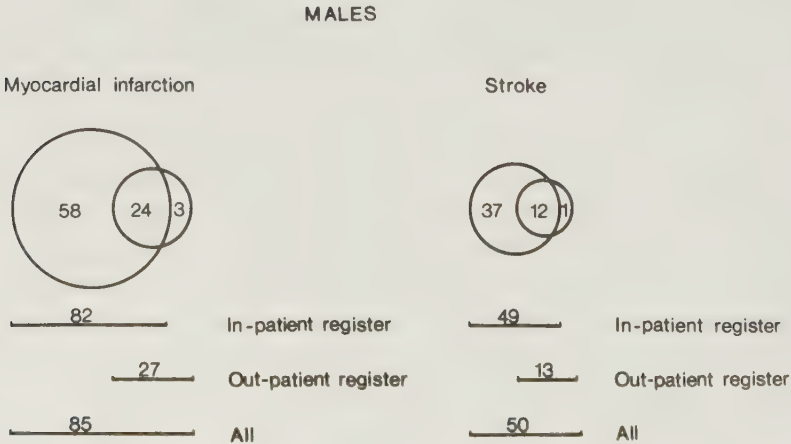


Figure 1. Number of male patients born between 1912 and 1931 with myocardial infarction or stroke during 1973-82, living in the Dalby primary care district. Registrations from the in-patient computer register compared with the out-patient register.

The medical records of all cases were sought and studied by a physician (LL). Information regarding the patients' smoking habits and diagnosis of hypertension - if any - was extracted. The numbers of male and female patients with myocardial infarction and stroke are shown in Figure 2.

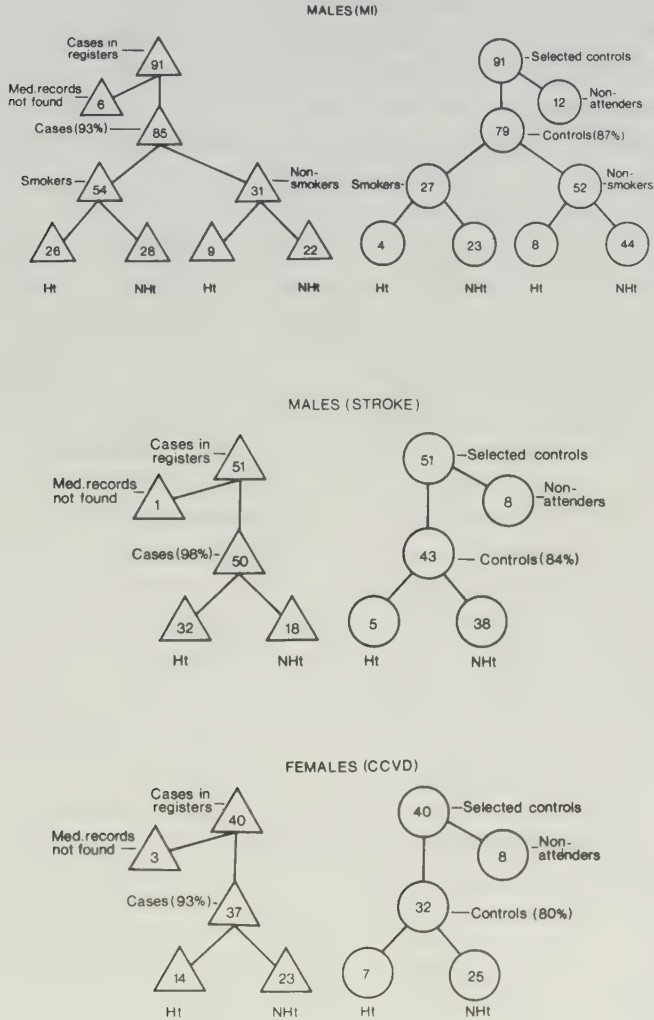


Figure 2. Patients born between 1912 and 1931 with myocardial infarction (**MI**, males), **stroke** (males), **CCVD** (females) and sex- and age-matched controls; Ht: hypertensives, NHT: non-hypertensives.

In 10 cases out of 182 (5 %) the medical records could not be found, which may be attributable to incorrect filing.

Controls

From earlier studies (1,2,13) we have obtained information about a control material representative of the population in our primary care district. This existing control material comprises 227 males and 250 females born in 1912-31 of whom 82 % attended examinations in 1981. The control material amounts to 16 % of all inhabitants in this age group in the district. It includes 12 male patients with a history of myocardial infarction and 6 with stroke as well as 4 female patients with myocardial infarction and one with stroke.

In the present case-control study we selected the controls from our existing control material. For each case we selected a control person who was as close in age as possible and of the same sex. When selecting controls for patients with myocardial infarction, those with a history of myocardial infarction themselves were omitted. The same exclusion procedure was performed with regard to stroke. The controls were not chosen at the time of diagnosis of the cases, since the bias introduced by ignoring the matching on time may be considered negligible when estimating risk (17).

The controls' smoking habits as well as their diagnosis of hypertension - if any - were known from our earlier studies. The numbers of controls in the different groups are shown in Figure 2. All comparisons were made between groups of cases and groups of controls.

Data processing and statistical methods

Data were stored, structured and analysed by using the SPSS Program System on a Univac 1100/80 Computer.

In order to test the differences between frequencies in two or more groups, the Chi-square test was used.

The relative odds were estimated and corrected for small numbers, as shown in Figure 3. The 95 % confidence limits were calculated as recommended by Lilienfeld (Haldane's method), (18).

	Cases	Controls
Hypertensives	a	b
Non-hypertensives	c	d

$$\psi = \frac{\frac{a}{b}}{\frac{c}{d}} = \frac{a \cdot d}{b \cdot c}$$

$$\psi_c = \frac{(a + 0.5) \cdot (d + 0.5)}{(b + 0.5) \cdot (c + 0.5)}$$

$$\lambda = \frac{p_e \cdot (R - 1)}{1 + p_e \cdot (R - 1)} \quad , \quad R = \psi_c$$

Figure 3. Relative odds (ψ), corrected relative odds (ψ_c), relative risk (R) and population attributable risk (λ) of disease in hypertensives vs. non-hypertensives; **a, b, c** and **d** indicate numbers; **p_e** indicates the prevalence of hypertension in the population.

The population-attributable risk was estimated as shown in Figure 3. It implies the impact that a specific exposure (hypertension) may have on the population with respect to a particular outcome (myocardial infarction or stroke). The prevalence of myocardial infarction in males in this age group could be roughly estimated to 6 % from the existing control material described above. The corresponding figure for stroke was likewise estimated to 3 %. Thus, the relative odds was considered approximately equal to the relative risk (Fig. 3). We have estimated the prevalence of hypertension in middle-aged males in the primary care district to about 15 % in earlier studies (1,2).

RESULTS

During the period 1973-82 there were 91 cases of myocardial infarction in males in this age group in the district (Fig. 2). The corresponding figure for females was 20. There were 51 cases of stroke in males and 20 in females.

Study of males with myocardial infarction

The relative odds (risk), corrected for small numbers, of myocardial infarction in males with hypertension was estimated to 3.8 (95 % confidence interval 1.8-8.0) as shown in Table I. When the estimates were calculated for smokers and non-smokers separately the odds of hypertension was higher in smoking males than in non-smokers 4.9 (1.6-15.2) and 2.2 (0.8-6.4) respectively. This procedure did not introduce any age bias into the material.

Table I. Relative odds (ψ_c) of myocardial infarction (MI) in smoking and non-smoking males born in 1912-1931 with vs without hypertension.

(95%): 95% confidence interval and λ : population attributable risk

	Cases (MI)	Controls (no-MI)	Rel. odds ¹ ψ_c (95%)	Pop. attrib. risk ² λ (%)
<i>All</i>				
hypertensives	35	12	3.8 (1.8-8.0)	30
non-hypertensives	50	67		
<i>Smokers</i>				
hypertensives	26	4	4.9 (1.6-15.2)	37
non-hypertensives	28	23		
<i>Non-smokers</i>				
hypertensives	9	8	2.2 (0.8-6.4)	15
non-hypertensives	22	44		

¹ corrected for small numbers

² prevalence of hypertension 0.15

The relative odds, corrected for small numbers, of myocardial infarction in smoking males was estimated to 3.3 (1.7-6.2) as shown in Table II. When the estimates were calculated for hypertensives and non-hypertensives separately the odds of smoking was higher in hypertensive males than in non-hypertensives, 5.3 (1.4-20.5) and 2.4 (1.1-5.1) respectively. The population-attributable risk of hypertension with respect to myocardial infarction was estimated to 30 % in all males, 37 % in smokers and 15 % in non-smokers (Table I).

Table II. Relative odds (ψ_c) of myocardial infarction (MI) in hypertensive and non-hypertensive males born in 1912-1931, with vs without the habit of smoking.

(95%): 95% confidence interval

	Cases (MI)	Controls (no-MI)	Rel. odds ¹ ψ_c (95%)
<i>All</i>			
smokers	54	27	3.3 (1.7-6.2)
non-smokers	31	52	
<i>Hypertensives</i>			
smokers	26	4	5.3 (1.4-20.5)
non-smokers	9	8	
<i>Non-hypertensives</i>			
smokers	28	23	2.4 (1.1-5.1)
non-smokers	22	44	

¹ corrected for small numbers

Study of males with stroke

The relative odds, corrected for small numbers, of stroke in males with hypertension was estimated to 12.3 (4.3-35.5) as shown in Table III. The population-attributable risk was estimated to 63 % in (all) males. These estimates were not calculated separately for smokers and non-smokers.

Table III. Relative odds (ψ_c) of stroke in males born in 1912-1931 with vs without hypertension. (95%): 95% confidence interval and λ : population attributable risk

	Cases (stroke)	Controls (no-stroke)	Rel. odds ¹ ψ_c (95%)	Pop. attrib. risk ² λ (%)
Hypertensives	32	5	12.3 (4.3-35.5)	63
Non-hypertensives	18	38		

¹ corrected for small numbers

² prevalence of hypertension 0.15

Table IV. Relative odds (ψ_c) of cerebro-cardiovascular disease (CCV) in females born in 1912-1931 with vs without hypertension.
(95%): 95% confidence interval

	Cases (CCV)	Controls (no-CCV)	Rel. odds ¹ ψ_c (95%)
Hypertensives	14	7	2.1 (0.7-5.9)
Non-hypertensives	23	25	

¹ corrected for small numbers

Study of females with myocardial infarction or stroke

As the number of female cases was small, we have analysed myocardial infarction and stroke combined as CCVD (Fig. 2).

The relative odds, corrected for small numbers, of CCVD in females with hypertension was estimated to 2.1 (0.7-5.9) as shown in Table IV. Chi-square was 2.0, N.S. The population-attributable risk was therefore not estimated in females. This study had a 75 % power to detect an excess risk of at least 3 (as in the Framingham study - see below) and a 60 % power to detect an excess risk of at least 2.5 in hypertensive females with regard to CCVD (prevalence of hypertension = 0.25 (19), one-sided $\alpha = 0.05$).

DISCUSSION

Our patients represented all new cases of myocardial infarction and stroke during a 10-year period who were born between 1912 and 1931 and were living in the Dalby district. They were identified by the in-patient computer scheme comprising all hospital admissions in the county as well as by the out-patient computer scheme comprising all visits to the health care centres in the district.

As can be seen in Figure 1 almost all male patients with acute myocardial infarction or stroke were admitted to hospital and most of them went there

directly without consulting the health care centres. We have no information, however, regarding patients who did not seek medical advice for these diseases (e.g. silent infarction) nor regarding those who died at home before being diagnosed.

The controls were selected in a known way from the population in the same primary care district as the cases and were matched for age, sex and race (all white).

Our results show hypertension and smoking to be independent risk indicators of myocardial infarction and accord with other prospective and larger studies (4,5,20). The odds ratio of stroke in hypertensive males was higher than the odds of myocardial infarction. This may be compared with the Framingham study where hypertension was the most common and potent precursor of atherothrombotic brain infarction (21). The risk of brain infarction in that study was about four times as high in hypertensives as in normotensives. The corresponding risk of ischaemic heart disease was about twice as high.

The excess risk of myocardial infarction and stroke in male hypertensives confirms earlier results on carefully treated male hypertensives in our district, in comparison with non-hypertensive controls, showing an odds ratio of CCVD amounting to 4.3-13.7 (1,13).

There were few cases of either myocardial infarction or stroke in females during the 10-year period. This was the case even though hypertension was more prevalent in females than in males in this age group. To avoid a type II fallacy it should be emphasized that the lack of significance may be attributed to the limited numbers. However, the result is in agreement with earlier retrospective studies on female hypertensives in comparison with non-hypertensive controls (1,13) and it is also supported by other studies (22).

The Framingham study, however, showed women to tolerate hypertension no better than men with respect to cerebrovascular disease (21), but for coronary heart disease the risk in females was about half of that in men (23).

The population-attributable risk of hypertension in the population, with regard to myocardial infarction and stroke in males, was estimated to 30 and 63 % respectively (Table I). This risk was higher in smoking (37 %) than in non-smoking (15 %) hypertensives, with regard to myocardial infarction. The concept of population-attributable risk is useful in that it provides an estimate

of the amount by which myocardial infarction and stroke might be reduced in the population in a primary care district if hypertension could be removed.

It may be noted that this primary care district has been subjected to extensive studies regarding blood pressure during the last decade (1,2,13,24). Few new hypertensives have been diagnosed in recent studies (1,13) and 75 % of the hypertensives were adhering to their treatment objectives. In the light of these results we conclude that our treatment of hypertension is unsatisfactory and ought to be supplemented by other measures in order to reduce the excess risks. In North Karelia, however, a community-based program has had a beneficial impact on lifestyle and cardiovascular risk factors on an entire population (25,26).

Our figures are in agreement with results obtained in large prospective studies (5,20-23,27). Thus, the present study has shown that a limited number of cases in a defined population can be utilized in epidemiological studies regarding risk and may therefore justify the case-control model for studies in primary health care.

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**BOTH HIGH AND LOW BLOOD PRESSURES FOUND TO BE RISK
INDICATORS OF DEATH**

Isotonic Regression of Blood Pressure on Age Applied to Data from a
13-year Prospective Study in Males

by

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SUMMARY

The study was performed to analyse the value of a 'casual' blood pressure as predictor of mortality.

Isotonic regression of blood pressure on age was performed and the individuals were thereafter ranked according to their excess blood pressures (positive or negative). Men in both extreme quintiles showed an excess death risk in comparison with those in the medium ones. At the time of the examination there were more men with chronic diseases among those who died in the lowest blood pressure quintile than among those who died in the other quintiles. An inhomogeneity was suggested for the low blood pressure group and also for the high one.

Key words: Blood pressure, death rate, isotonic regression, prospective studies.

INTRODUCTION

It is well known that hypertensives are especially prone to cerebro-cardiovascular disease (CCVD) and premature death and it is also well known that there is a strong relationship between the level of blood pressure and CCVD (1-3).

The predictive value of systolic blood pressure is generally considered greater than that of diastolic pressure (2). However, most studies on the benefit of treatment of patients with either established or mild hypertension are based on diastolic blood pressure (4-6).

Even isolated 'casual' blood pressure recordings are considered sufficiently reliable predictors of premature death to be used by insurance companies when estimating risk (3) and it has recently been suggested in a 26-year follow-up of the Framingham study, that it is the actual level of blood pressure, and not its trend in the past, that should be considered when deciding on treatment in patients with established or borderline hypertension (7).

Earlier retrospective studies in the Dalby population have shown high risks of CCVD in hypertensives in comparison with non-hypertensive controls, even though 75 % of the former attained their treatment objectives (8,9), which were in accordance with internationally accepted norms.

In 1969-70 all residents of Dalby village (954 male and 963 female) who were 8 years old or more were invited to an ophthalmic examination which also included a blood pressure recording. Thus, 'casual' blood pressure recordings were available on a defined population followed for 13 years and subjected to registration of morbidity and mortality in an out-patient as well as in an in-patient computer scheme (10,11).

Prospective studies on mortality as a function of blood pressure often comprise large age cohorts (12,13) or large populations (1-3,14). Against this background we found it of interest to analyse the predictive value of the 'casual' blood pressure recordings made in 1969-70 regarding mortality in the males in our defined population, for which the primary health care scheme is responsible.

METHODS

Study population

The subjects were derived from a general ophthalmic population survey carried out by one of the authors (B.B.) at the Dalby Health Care Centre in southwest Sweden from March 1969 to April 1970. Invitations with an appointment notification and a brief questionnaire were mailed in rotation, using a directory, to all persons aged 8 years or more, who had been residents of the village surrounding the Health Care Centre since December 1968. The fact that a measurement of the blood pressure was part of the examination was not mentioned in the invitation. The questionnaire included one question regarding medications currently being used.

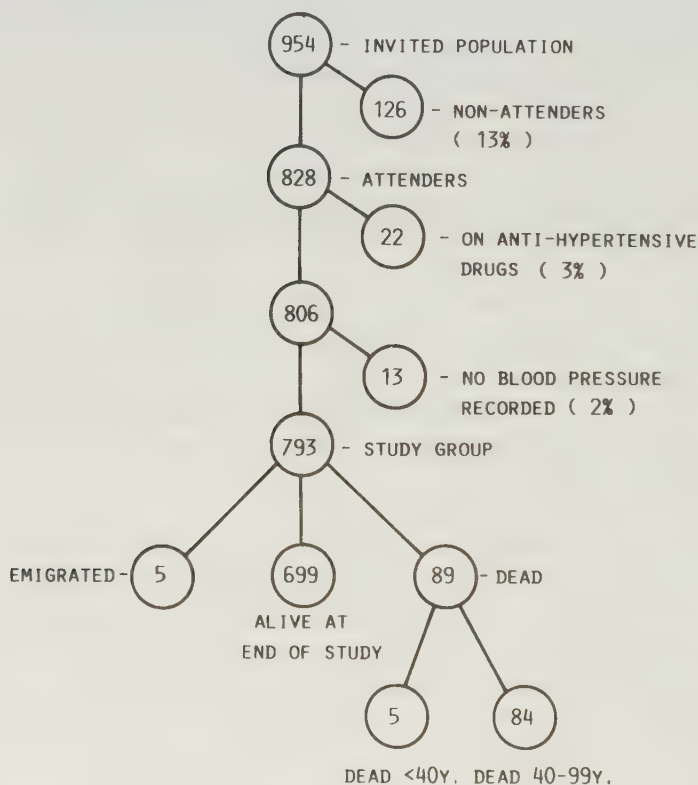


Figure 1. Male Dalby population aged 8 years and above invited to our ophthalmic examination in 1969-70 and followed up for 13 years.

Of 954 males invited, 828 (87 %) took part in the survey (Fig. 1). Twenty-two men using drugs listed in the Swedish Pharmacopoeia of 1969 under the heading "Agents in Hypertension" (15) were excluded from the present study, since we regarded their blood pressures as 'artificially' depressed and not representative of their 'true' blood pressures. For various reasons blood pressures were not measured in 13 males; hence the study group totalled 793 males (83 %). The attendance has been carefully described elsewhere (10,11). It was high (over 80 %) even among those aged 80 years and more.

Organization

The systolic and diastolic (phase V) blood pressures were measured in the right arm immediately after the subject had assumed a recumbent position. One single mercury manometer with cuffs of different sizes (16) was used. The readings were determined to the nearest 5 mm Hg. All measurements were made by the same nurse. All data were immediately recorded on special forms.

Information about deaths was obtained continuously from the Dalby Parish Office which has the primary responsibility for the census register in Dalby, as well as from the National Central Bureau of Statistics. It was based on necropsy (64 %) and death certificates (36 %) and diagnoses were coded according to the ICD (International Statistical Classification of Diseases) codes (17). CCVD was identified by ICD codes 400-445. Probands who emigrated were followed until their emigration date.

Non-attenders

The death rates among the male non-attenders were compared with those of the attenders. In the age group 40-69 years the non-attenders showed a death risk of 2.2 (SE 0.9) vis-à-vis the attenders. In those aged 40-99 years the corresponding figure was 1.9 (SE 0.5).

The medical records of the deceased non-attenders aged 40 years or more at the time of the survey (n=19) were sought and studied regarding diseases they may have suffered from in 1969-70. Their records were found in 15 cases (79 %) and 9 had been suffering from a chronic disease at the time of the survey.

Excluded probands

Of 22 males excluded because of antihypertensive drug treatment, 16 died during the observation period, 8 from a CCVD. All but 5 died after reaching the age of 70 years.

The death rates among the excluded probands were compared with those of the included. In the age group 40-69 years the excluded showed a death risk of 4.7 (SE 2.3) vis-à-vis the included. In those aged 40-99 years the corresponding figure was 2.1 (SE 0.6). It should be emphasized, however, that the first of these figures (age group 40-69 years) is founded on information from only 73 person-years, and hence negligible in comparison with 4,336 person-years among the included.

Epidemiological and statistical methods

In order to study the influence of blood pressure level on mortality, a regression analysis of blood pressure on age was first performed; the reason for this was that we deemed it necessary to relate the blood pressure measurement actually obtained from a proband to the "normal" blood pressure for a man of that age. As it is known that blood pressure increases with age, isotonic regression was considered a more adequate method than using either one or more single regression lines or a higher degree polynomial. Isotonic regression is a method which amounts to finding that increasing function which in the least-squares sense best approximates the points in the data set, as described by Barlow et al (18). Such a regression, which is necessarily performed on a computer, produces a function which is not expressed by any explicit formula but rather in the form of a table or a graph (cf. Figures 2 and 3). In order to form each proband's **absolute excess pressure** (positive or negative), the difference between his actual recording and the value predicted by the regression curve was calculated.

The individuals were then ranked according to their excess pressures and divided into quintiles. The first quintile (low-pressure group) and the fifth quintile (high-pressure group) were both compared with a third group (medium-pressure group) formed by the three medium quintiles. When two persons had equal excess pressures the older one was considered to have the lower excess pressure.

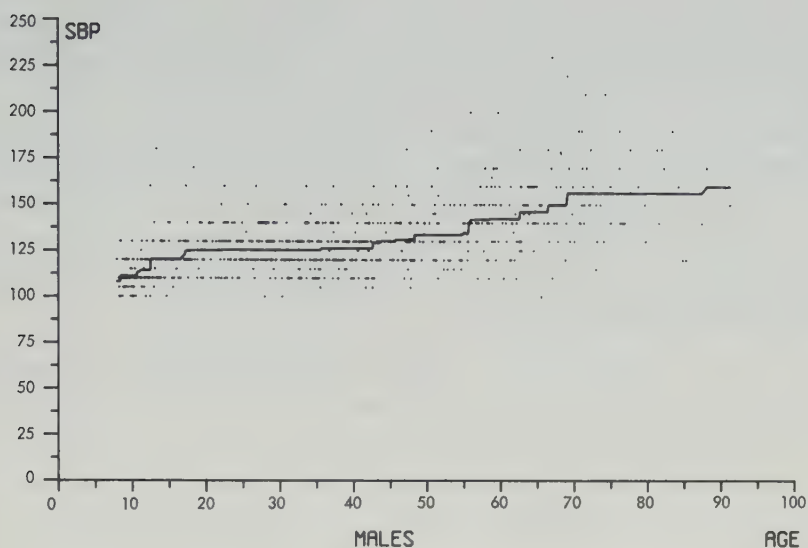


Figure 2. Recorded systolic blood pressures and their isotonic regression on age in 793 males.

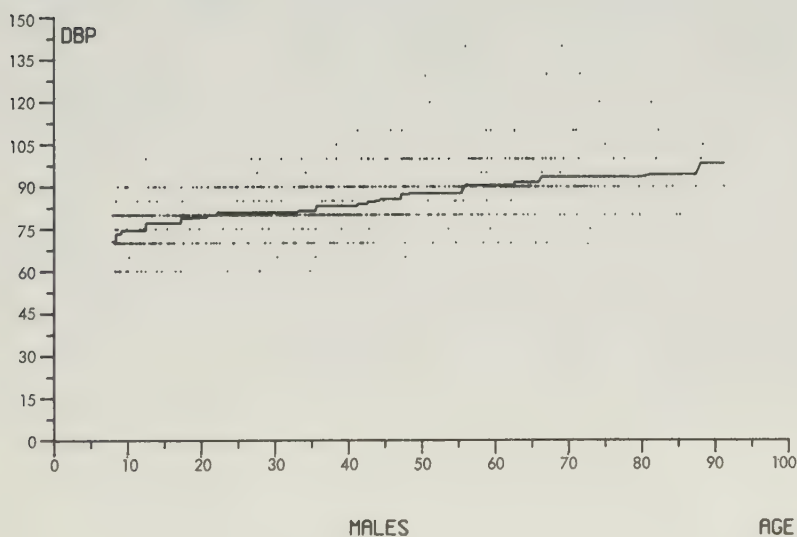


Figure 3. Recorded diastolic blood pressures and their isotonic regression on age in 793 males.

As the variation in blood pressure usually is higher in older ages, the method used might produce more older persons in the extreme groups than in the medium one. To circumvent this, the normal variation $\sigma(a)$ at age a was estimated - in fact by using isotonic regression of the absolute residuals on age -, and the absolute excess pressure was standardized by dividing it by $\sigma(a)$; the quantity so obtained was called a **standardized excess pressure** . Both quantities described - absolute and standardized excess pressure - have been used in the analyses. Details about this application of isotonic regression will be published separately (19).

The number of person-years at risk and the observed number of deaths were calculated for each of the three blood pressure groups and within each 5-year age interval. Indirect standardization was performed, using death rates for Malmöhus County minus Greater Malmö Area, in order to compensate for possible differences in age structure between the blood pressure groups. Thus, first a standardized mortality ratio and then a death rate were obtained for each group.

The standardized death rates of the low and high blood pressure groups were divided by that of the medium one, giving an age-adjusted mortality ratio relative to that group. When some of the calculations were repeated using one-year age intervals instead of 5-year intervals the differences were negligible. The calculations described for overall mortality regarding absolute excess pressure were also performed for mortality in CCVD.

In order to separate early and late deaths in the low blood pressure group, analyses were performed separately for the first and the second half of the 13-year observation period.

Statistical significance was assessed, concerning death rates and mortality ratios, using two-sided tests and normal approximation, assuming Poisson variation among observed deaths. The Chi-square test was used to test the difference between frequencies in two groups. The Yates' correction for continuity was thereby used.

RESULTS

Eighty-nine men died during the 13-year observation period (11.2 %): 84 in the age group 40-99 years and 29 in the age group 40-69 years. The corresponding figures for deaths in CCVD were 45, 44 and 14, respectively.

Men in both extreme groups showed an excess death risk in comparison with those of the medium group, as can be seen from Table I and Figure 4. This was so regardless of whether absolute or standardized excess blood pressure was analysed and regardless of whether systolic or diastolic pressure was considered. The excess risks were higher in the age group 40-69 years than in the age group 40-99 years.

When deaths due to CCVD were analysed, the results were similar to those for total deaths for the age group 40-69 years (Table II and Figure 5) but not for the age group 40-99 years (Table II).

The death risk in the low blood pressure group relative to the medium one in age group 40-69 years was 3.5 (SE 2.1) when computed for the first half of the observation period and 1.6 (SE 1.0) for the second half. The corresponding figures for the high blood pressure group relative to the medium one were 2.9 (SE 1.9) and 0.9 (SE 0.7), respectively. The figures were lower but the trend similar although less pronounced when we analysed the entire age group 40-99 years.

None of the comparisons of death risk given above and in Tables I-II reached statistical significance at the 5 % level, two-tailed tests.

The medical records of the men who died in the age group 40-99 years (n=84) were sought and studied regarding which chronic disease(s) they may have been suffering from at the time of the examination in 1969-70. Their records were found in 70 cases (83 %). Twenty-six (37 %) had a chronic disease: 17 CCVD, 12 chronic bronchitis and 5 malignant neoplasm(s). When analysed separately for the three blood pressure groups (Table III) there were more men with chronic disease ($p < 0.001$) and CCVD ($p < 0.01$) in the low blood pressure group than in the other groups.

Table 1. Death rates per 10 000 person years (p.y.) for males aged 40-69 and 40-99 years with low, medium and high absolute excess blood pressure (AEBP) and standardized excess blood pressure (SEBP) and mortality ratios relative to the medium blood pressure group.

	40 - 69 years		40 - 99 years	
	Death rate per 10 000 p.y. (SE)	Mortality ratio (SE)	Death rate per 10 000 p.y. (SE)	Mortality ratio (SE)
Systolic AEBP				
Low	135 (37)	2.9 (1.3)	239 (44)	1.4 (0.4)
Medium	46 (15)	-	167 (30)	-
High	89 (34)	1.9 (1.0)	250 (50)	1.5 (0.4)
Systolic SEBP				
Low	131 (42)	2.4 (1.0)	236 (57)	1.2 (0.3)
Medium	55 (16)	-	196 (28)	-
High	95 (36)	1.7 (0.8)	223 (51)	1.1 (0.3)
Diastolic AEBP				
Low	120 (38)	2.3 (1.0)	258 (59)	1.5 (0.4)
Medium	53 (16)	-	171 (25)	-
High	102 (36)	1.9 (0.9)	313 (70)	1.8 (0.5)
Diastolic SEBP				
Low	128 (40)	2.5 (1.1)	265 (61)	1.6 (0.4)
Medium	51 (15)	-	168 (25)	-
High	106 (37)	2.1 (1.0)	319 (71)	1.9 (0.5)

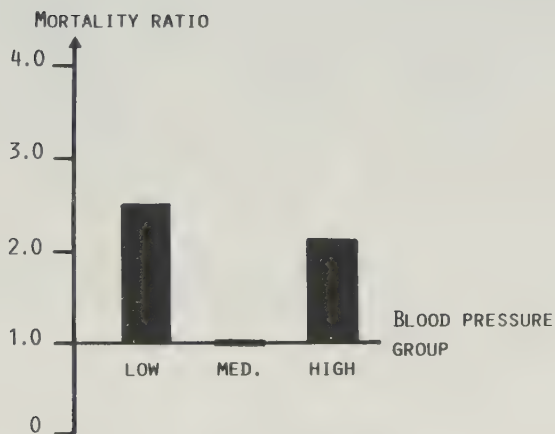
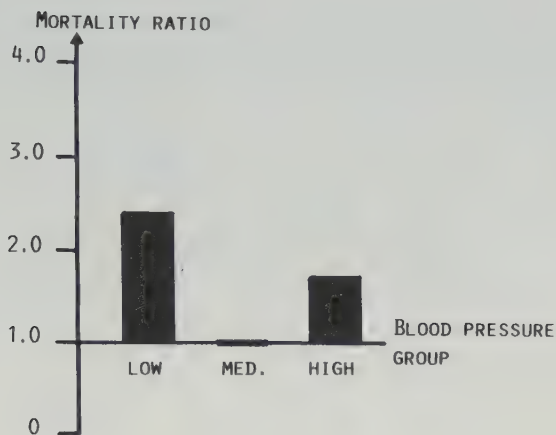


Figure 4. Mortality ratios (total deaths, 13-year follow-up) in ages 40-69 years of low and high blood pressure groups relative to the medium group; systolic standardized excess pressure (above) and diastolic standardized excess pressure (below).

Table II. Cerebro-cardiovascular death rates per 10 000 person years (p.y.) for males aged 40-69 and 40-99 years with low, medium and high absolute excess blood pressure (AEBP) and mortality ratios relative to the medium blood pressure group.

	40 - 69 years		40 - 99 years	
	Death rate per 10 000 p.y. (SE)	Mortality ratio (SE)	Death rate per 10 000 p.y. (SE)	Mortality ratio (SE)
Systolic AEBP				
Low	73 (28)	3.4 (2.1)	108 (30)	1.0 (0.3)
Medium	22 (11)	-	113 (26)	-
High	39 (23)	1.8 (1.4)	122 (35)	1.1 (0.4)
Diastolic AEBP				
Low	62 (28)	2.5 (1.6)	100 (38)	1.0 (0.4)
Medium	25 (11)	-	100 (20)	-
High	54 (27)	2.2 (1.4)	188 (57)	1.9 (0.7)

Table III. Frequency (%) of chronic disease at the examination in those males who died aged 40-99 years (data available on 70 out of 84).

p indicates the level of significance, chi sq test.

	Frequency (%)			P		
	Low BP (n=24)	Med BP (n=24)	High BP (n=22)			
	L	M	H	Lvs.M	Lvs.H	Mvs.H
Chronic disease	71	21	18	<0.001	<0.001	N.S.
- CCVD	46	8	18	<0.01	<0.05	N.S.
- Chronic bronchitis	29	12	9	N.S.	N.S.	N.S.
- Malignant neoplasm(s)	17	4	0	N.S.	N.S.	N.S.
No chronic disease	29	79	82			

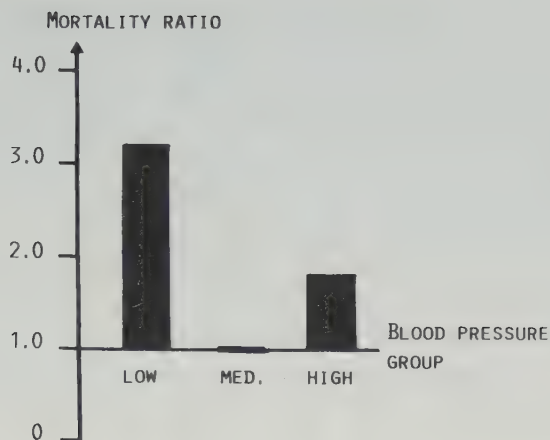


Figure 5. Mortality ratios (deaths from CCVD, 13-year follow-up) in ages 40-69 years of low and high blood pressure groups relative to the medium group; systolic absolute excess pressure.

DISCUSSION

Men in both extreme groups showed an excess death risk in comparison with those of the medium group; thus, mortality was a U-shaped function of excess blood pressure (as defined above). The study comprised deaths in men from the age of 40 years who were observed over a 13-year period. There were few deaths and comparisons of death risks did not reach statistical significance at the 5 % level. However, all comparisons in the age group 40-69 years and most in the group 40-99 years pointed in the same direction, thus supporting a very strong trend.

When analysing total mortality it is important to consider the characteristics of the population being studied, since different risk factors may be important to different subgroups. The most interesting result of our study was the high death

rate among men in the **low** blood pressure group in comparison with the medium one (Tables I, II). When the calculations were performed separately for the first and the second half of the observation period, the mortality ratio of the low blood pressure group vis-à-vis the medium one was higher during the first half. In other words, there were more early deaths than late ones in the low blood pressure group, thus indicating an inhomogeneity in this group. When the medical records of the deceased were extracted and studied (Table III), 71 % of the dead men in the low pressure group had suffered from a chronic disease (CCVD, chronic bronchitis, or malignant neoplasm) at the time of the examination, in comparison with 21 % of those in the medium group. Almost half of the dead men in the low pressure group had suffered from a CCVD before the examination. These results tally with the high early death rate in the low pressure group.

In the **high** blood pressure group there was also an excess death risk when compared with the medium group. This difference was explained by deaths during the first half of the observation period, thus suggesting an inhomogeneity in the former group; however, examination of the records provided no further insight (Table III).

The over-mortality in our high pressure group accords with the Framingham (2) and other studies (1,3,12,14). The Framingham study did, however, not show any U-shaped mortality curve, this may be explained by the fact that persons with CCVD at entry were excluded from that study which furthermore only comprised two-thirds of the random sample invited. In the Bergen study (14) the age-specific total death rate in men showed a general increase with increasing systolic blood pressure, while the corresponding curve for diastolic blood pressure was more U-shaped. The curves were clearly U-shaped in women in the Bergen study.

In prospective studies on middle-aged women in Gothenburg (13) there was a tendency towards a U-shaped pattern for CCVD as a function of blood pressure. There was, however, no obvious U-shaped pattern regarding mortality in that study.

Male patients receiving antihypertensive treatment were excluded from our study for reasons given above. If they had been included they might have influenced the results of the age group 40-99 years, but hardly those of the 40 to 69 year group, as discussed in Methods.

Our study group comprised all males in a defined rural-suburban area, who were 8 years old or more when they attended an ophthalmic survey. The attendance was very high also among those aged 80 years and above, possibly because the elderly were inclined to have their sight examined. The death rates in our male non-attenders above the age of 40 years were twice as high as in those who attended, which tallies with other studies (20,21). We found no indicators of alcohol-related death among our non-attenders, who in many cases were bed-ridden at the time of the invitation.

Serum-cholesterol has been shown to be reciprocally correlated to cancer deaths and alcohol-related deaths and strongly positively correlated to death from coronary heart diseases, thus giving rise to a U-shaped mortality curve (22,23). A U-shaped pattern has also been reported for body-mass index (weight/height²) and mortality (24), which persisted unchanged also after the first years of observation. The mortality explaining this phenomenon was characterized by typical "low-weight causes" (tuberculosis, lung cancer, obstructive lung disease and stomach cancer) and typical "high-weight causes" (CCVD, diabetes and colon cancer). Recent data from the Framingham study (25) indicate that the U-shaped curve describing the association between weight and mortality could be explained by the fact that smokers were 1.5 times as common in the underweight part of the distribution as in the overweight.

In our study of deceased men there were no differences in body-mass index at the time of the examination in the three blood pressure groups (25.8, 25.7 and 26.9, respectively). There were, however, more ($p < 0.05$) men suffering from chronic bronchitis in the low blood pressure group than in the other two groups pooled, which may be indicative of more smoking in the former group.

Finally, let us comment on the epidemiological methods used. Our ways of estimating and comparing mortality in the different groups are the standard ones. However, the technique of defining our groups is new to the best of our knowledge; in particular we have found the use of isotonic regression advantageous: even if we do not claim that isotonic regression is an indispensable tool, we do contend that it simplifies the analyses and relieves the physician and the statistician from troublesome decisions such as choice of polynomial degree, choice of interval end-points for age grouping, choice of whether or not a piecewise linear regression function should be continuous or not.

A disadvantage with isotonic regression, however, is that it presupposes the variable under study (in our case the blood pressure) to be monotonically increasing or, at worst, constant. In our material there was in fact a slight decrease in mean blood pressure in the highest age group (73 years and above; $n=29$) which we disregarded.

In our opinion, the technique used in this study is particularly relevant in connection with moderately sized materials like ours.

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